IN THE UNITED STATES DISTRICT COURT

FOR THE DISTRICT OF DELAWARE

SIGHT SCIENCES, INC., Plaintiff, v. IVANTIS, INC., ALCON RESEARCH LLC, ALCON VISION, LLC, and ALCON INC., Defendants.	)	**Redacted - Public Version** C.A. No. 21-1317-GBW-SRF [redacted]

DECLARATION OF NOAH FRANK IN SUPPORT OF DEFENDANTS' MOTION TO EXCLUDE AND MOTION FOR SUMMARY JUDGMENT

I, Noah Frank, declare as follows:

1. I am a partner at the law firm of Kirkland & Ellis, LLP, counsel for Defendants in the above captioned matter. I am admitted to practice before the Court pro hac vice. I submit this declaration in support of Defendants' Motion to Exclude and Motion for Summary Judgment.

2. Attached hereto as Exhibit 1 is a true and accurate copy of U.S. Patent No. 8,287,482.

3. Attached hereto as Exhibit 2 is a true and accurate copy of U.S. Patent No. 9,370,443.

4. Attached hereto as Exhibit 3 is a true and accurate copy of U.S. Patent No. 9,486,361.

5. Attached hereto as Exhibit 4 is a true and accurate copy of U.S. Patent No. 10,314,742.

6. Attached hereto as Exhibit 5 is a true and accurate copy of U.S. Patent No. 11,389,328.

7. Attached hereto as Exhibit 6 is a true and accurate copy of Non-Final Office Action, excerpted from the certified file history for U.S. Patent No. 10,314,742, bearing beginning Bates Number SGHT0006176, and highlighted for the Court's convenience.

8. Attached hereto as Exhibit 7 is a true and accurate copy of Response to Non-Final Office Action, excerpted from the certified file history for U.S. Patent No. 10,314,742, and highlighted for the Court's convenience.

9. Attached hereto as Exhibit 8 is a true and accurate copy of Non-Final Office Action, excerpted from the certified file history for U.S. Patent No. 11,389,328, bearing beginning Bates Number SGHT0007428, and highlighted for the Court's convenience.

10. Attached hereto as Exhibit 9 is a true and accurate copy of Response to Non-Final Office Action, excerpted from the certified file history for U.S. Patent No. 11,389,328, and highlighted for the Court's convenience.

11. Attached hereto as Exhibit 10 is a true and accurate copy of the Opening Expert Report of John C. Jarosz, served on July 13, 2023, and highlighted for the Court's convenience. [FILED UNDER SEAL].

12. Attached hereto as Exhibit 11 is a true and accurate copy of the Reply Expert Report of John C. Jarosz, served on September 7, 2023, and highlighted for the Court's convenience. [FILED UNDER SEAL].

13. Attached hereto as Exhibit 12 is a true and accurate copy of the Expert Report of Professor David Gal, Ph.D., served on August 17, 2023, and highlighted for the Court's convenience. [FILED UNDER SEAL].

14. Attached hereto as Exhibit 13 is a true and accurate copy of the Expert Rebuttal Report of Paul K. Meyer, served on August 17, 2023, and highlighted for the Court's convenience. [FILED UNDER SEAL].

15. Attached hereto as Exhibit 14 is a true and accurate copy of the Opening Expert Report of Dr. J. Crawford Downs on Infringement of U.S. Patent Nos. 8,287,482; 9,370,443; 9,486,361; 10,314,742; and 11,389,328, served on July 13, 2023, and highlighted for the Court's convenience. [FILED UNDER SEAL].

16. Attached hereto as Exhibit 15 is a true and accurate copy of the Corrected Rebuttal Expert Report of Dr. J. Crawford Downs on Invalidity of U.S. Patent Nos. 8,287,482; 9,370,443; 9,486,361; 10,314,742; and 11,389,328, served on August 22, 2023, and highlighted for the Court's convenience. [FILED UNDER SEAL].

17. Attached hereto as Exhibit 16 is a true and accurate copy of the Reply Expert Report of Dr. J. Crawford Downs on Infringement of U.S. Patent Nos. 8,287,482; 9,370,443; 9,486,361; 10,314,742; and 11,389,328, served on September 7, 2023, and highlighted for the Court's convenience. [FILED UNDER SEAL].

18. Attached hereto as Exhibit 17 is a true and accurate copy of the Opening Expert Report of Angelo P. Tanna, M.D. on Invalidity of U.S. Patent Nos. 8,287,482; 9,370,443; 9,486,361; 10,314,742; and 11,389,328 (corrected), dated on July 13, 2023, and highlighted for the Court's convenience. [FILED UNDER SEAL].

19. Attached hereto as Exhibit 18 is a true and accurate copy of the Reply Expert Report of Angelo P. Tanna, M.D. on Invalidity of U.S. Patent Nos. 8,287,482; 9,370,443; 9,486,361; 10,314,742; and 11,389,328, served on September 7, 2023, and highlighted for the Court's convenience. [FILED UNDER SEAL].

20. Attached hereto as Exhibit 19 is a true and accurate copy of the Rebuttal Expert Report of Andrew G. Iwach, M.D., served August 17, 2023, and highlighted for the Court's convenience. [FILED UNDER SEAL].

21. Attached hereto as Exhibit 20 is a true and accurate copy of excerpts from Mark Papini's Deposition Transcript, taken on August 2 and 3, 2023, and highlighted for the Court's convenience. [FILED UNDER SEAL].

22. Attached hereto as Exhibit 21 is a true and accurate copy of excerpts from Doug Roeder's Deposition Transcript, taken on June 21, 2023, and highlighted for the Court's convenience. [FILED UNDER SEAL].

23. Attached hereto as Exhibit 22 is a true and accurate copy of excerpts from John Jarosz's Deposition Transcript, taken on September 13, 2023, and highlighted for the Court's convenience. [FILED UNDER SEAL].

24. Attached hereto as Exhibit 23 is a true and accurate copy of excerpts from J. Crawford Downs's Deposition Transcript, taken on September 22, 2023, and highlighted for the Court's convenience. [FILED UNDER SEAL].

25. Attached hereto as Exhibit 24 is a true and accurate copy of excerpts from J. Crawford Downs's Deposition Transcript, taken on September 28, 2023, and highlighted for the Court's convenience. [FILED UNDER SEAL].

26. Attached hereto as Exhibit 25 is a true and accurate copy of excerpts from David Badawi's Deposition Transcript, taken on June 12, 2023, and highlighted for the Court's convenience. [FILED UNDER SEAL].

27. Attached hereto as Exhibit 26 is a true and accurate copy of excerpts from Paul Badawi's Deposition Transcript, taken on June 23 and 26, 2023, and highlighted for the Court's convenience. [FILED UNDER SEAL].

28. Attached hereto as Exhibit 27 is a true and accurate copy of excerpts from David Van Meter's Deposition Transcript, taken on June 27, 2023, and highlighted for the Court's convenience. [FILED UNDER SEAL].

29. Attached hereto as Exhibit 28 is a true and accurate copy of excerpts from Paul Meyer's Deposition Transcript, taken on September 27, 2023, and highlighted for the Court's convenience. [FILED UNDER SEAL].

30. Attached hereto as Exhibit 29 is a true and correct copy of emails between David Badawi and Admedes, bearing Bates numbers ADMEDES00115-116 and highlighted for the Court's convenience. [FILED UNDER SEAL].

31. Attached hereto as Exhibit 30 is a true and accurate copy of Glaukos and Ivantis's Settlement Agreement, bearing Bates numbers GK00000001-27 and highlighted for the Court's convenience. [FILED UNDER SEAL].

32. Attached hereto as Exhibit 31 is a true and correct copy of International Publication WO 2005/105197 A2 (Lynch-197), bearing Bates numbers IVANTIS_SS_00002554-611 and highlighted for the Court's convenience.

33. Exhibit 32 is left intentionally blank.

34. Attached hereto as Exhibit 33 is a true and accurate copy of Ivantis's "Hydrus Microstent: Product Positioning & Key Messaging" presentation, bearing Bate numbers IVANTIS_SS_00004424-44 and highlighted for the Court's convenience. [FILED UNDER SEAL].

35. Attached hereto as Exhibit 34 is a true and accurate copy of article "Ivantis Announces Settlement of Glaukos Patent Litigation" (2021), bearing Bates numbers IVANTIS_SS_00009130-32 and highlighted for the Court's convenience.

36. Attached hereto as Exhibit 35 is a true and accurate copy of article "Ivantis Announces FDA Approval for Its Innovative Hydrus Microstent Device for Minimally Invasive Glaucoma Surgery (MIGS)" (2018), bearing Bates number IVANTIS_SS_00010599-601 and highlighted for the Court's convenience. [FILED UNDER SEAL].

37. Attached hereto as Exhibit 36 is a true and accurate copy of Ivantis's "Ivantis Overview: For Alcon" presentation, bearing Bates numbers IVANTIS_SS_00011409-511. [FILED UNDER SEAL].

38. Attached hereto as Exhibit 37 is a true and accurate copy of Market Scope US Glaucoma Quarterly Update Q1 – 2019, bearing Bates numbers IVANTIS_SS_00013107-30. [FILED UNDER SEAL].

39. Exhibit 38 is left intentionally blank.

40. Attached hereto as Exhibit 39 is a true and accurate copy of excerpts from Ivantis's "Hydrus Microstent Global Training" presentation, bearing Bates numbers IVANTIS_SS_00044472-721 and highlighted for the Court's convenience. [FILED UNDER SEAL].

41. Attached hereto as Exhibit 40 is a true and accurate copy of Ivantis's "Ivantis Overview" presentation, bearing Bates numbers IVANTIS_SS_00091343-484. [FILED UNDER SEAL].

42. Attached hereto as Exhibit 41 is a true and correct copy of article "Trabecular Bypass Stents Decrease Intraocular Pressure in Cultured Human Anterior Segments" (Bahler 2004), bearing Bates numbers IVANTIS_SS_00159866-874.

43. Attached hereto as Exhibit 42 is a true and accurate copy of excerpts from the Option Agreement and Plan of Merger between Alcon and Ivantis, dated November 9, 2018, bearing Bates numbers IVANTIS_SS_00169590-956 and highlighted for the Court's convenience. [FILED UNDER SEAL].

44. Attached hereto as Exhibit 43 is a true and accurate copy of excerpts from David Van Meter's Deposition Transcript from the Glaukos Litigation, taken on September 26, 2019,

bearing Bates numbers IVANTIS_SS_00172370 and highlighted for the Court's convenience. [FILED UNDER SEAL].

45. Attached hereto as Exhibit 44 is a true and accurate copy of Alcon's "2021 Strategy & Outlook" presentation, bearing Bates numbers IVANTIS_SS_00204870-88. [FILED UNDER SEAL].

46. Attached hereto as Exhibit 45 is a true and accurate copy of Alcon's "Marketing: Strategy, Messaging, Assets, Objection Handling" presentation, bearing Bates numbers IVANTIS_SS_00324043-116. [FILED UNDER SEAL].

47. Attached hereto as Exhibit 46 is a true and accurate copy of Amendment No. 1 to Option Agreement and Plan of Merger between Alcon and Ivantis, bearing Bates numbers IVANTIS_SS_00420568-77 and highlighted for the Court's convenience. [FILED UNDER SEAL].

48. Attached hereto as Exhibit 47 is a true and accurate copy of Alcon's Memorandum regarding the Ivantis, Inc. Acquisition, bearing Bates numbers IVANTIS_SS_00445917-24 and highlighted for the Court's convenience. [FILED UNDER SEAL].

49. Attached hereto as Exhibit 48 is a true and accurate copy of Alcon's "Hydrus Adopter, Rejector & Aware Qualitative Exploratory Research" presentation, bearing Bates numbers IVANTIS_SS_00446528-613. [FILED UNDER SEAL].

50. Attached hereto as Exhibit 49 is a true and correct copy of article "EyePass glaucoma device shows promise," bearing Bates numbers IVANTIS_SS_00456103-104 and highlighted for the Court's convenience.

51. Attached hereto as Exhibit 50 is a true and accurate copy of Sight Sciences's Questionnaire of Sales Representatives, bearing Bates number IVANTIS_SS_00470628.

52. Attached hereto as Exhibit 51 is a true and accurate copy of Sight Sciences's National Institute of Health Grant Application, bearing Bates numbers SGHT0026782-845 and highlighted for the Court's convenience. [FILED UNDER SEAL].

53. Attached hereto as Exhibit 52 is a true and accurate copy of emails between Paul Badawi and Walter Fabisiak, bearing Bates numbers SGHT0030772-774. [FILED UNDER SEAL].

54. Attached hereto as Exhibit 53 is a true and accurate copy of a National Institute of Health's Response to Sight Sciences's Grant Application, bearing Bates numbers SGHT0116857-866. [FILED UNDER SEAL].

55. Attached hereto as Exhibit 54 is a true and accurate copy of an email between David Badawi and Mayo Clinic, bearing Bates numbers SGHT0161700 and highlighted for the Court's convenience. [FILED UNDER SEAL].

56. Attached hereto as Exhibit 55 is a true and accurate copy of Mayo Clinic's stent IOP reduction study results, bearing Bates numbers SGHT0161701-703 and highlighted for the Court's convenience. [FILED UNDER SEAL].

57. Attached hereto as Exhibit 56 is a true and accurate copy of the responses to Sight Science's Questionnaire of Sales Representatives, bearing Bates number SGHT0166268 and highlighted for the Court's convenience. [FILED UNDER SEAL].

58. Attached hereto as Exhibit 57 is a true and accurate copy of emails between Alisa Foster and Mark Papini, bearing Bates numbers SGHT0170173-4 and highlighted for the Court's convenience. [FILED UNDER SEAL].

59. Attached hereto as Exhibit 58 is a true and accurate copy of Plaintiff's Objections and Responses to Defendants' Third Set of Interrogatories (Nos. 11-18), served on May 1, 2023, and highlighted for the Court's convenience. [FILED UNDER SEAL].

60. Attached hereto as Exhibit 59 is a true and accurate copy of Plaintiff's First Supplemental Objections and Responses to Defendants' Second Set of Requests for Admission, served on August 15, 2023, and highlighted for the Court's convenience. [FILED UNDER SEAL].

61. Attached hereto as Exhibit 60 is a true and accurate copy of excerpts from the Markman Hearing Transcript, dated February 9, 2023, and highlighted for the Court's convenience. [FILED UNDER SEAL].

62. Attached hereto as Exhibit 61 is a true and accurate copy of excerpts from Petition for Inter Partes Review (Paper 2) in IPR2022-01529, dated September 12, 2022, and highlighted for the Court's convenience.

63. Attached hereto as Exhibit 62 is a true and accurate copy of excerpts from Petition for Inter Partes Review (Paper 2) in IPR2022-01540, dated September 16, 2022, and highlighted for the Court's convenience.

64. Attached hereto as Exhibit 63 is a true and accurate copy of excerpts from Patent Owner's Preliminary Response (Paper 6) in IPR2022-01529, dated December 23, 2022, and highlighted for the Court's convenience.

65. Attached hereto as Exhibit 64 is a true and accurate copy of excerpts from Patent Owner's Preliminary Response (Paper 6) in IPR2022-01540, dated December 28, 2022, and highlighted for the Court's convenience.

66. Attached hereto as Exhibit 65 is a true and accurate copy of Plaintiff's Second Supplemental Responses and Objections to Defendants' Interrogatory No. 8, dated May 25, 2023, and highlighted for the Court's convenience. [FILED UNDER SEAL].

I declare under penalty of perjury that the foregoing is true and correct, and that this declaration was executed on October 12, 2023.

/s/ Noah Frank
Noah Frank

CERTIFICATE OF SERVICE

I, Andrew E. Russell, hereby certify that on October 12, 2023, this document was served on zsightsciencesivantis@cooley.com and the persons listed below in the manner indicated:

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EXHIBIT 1

US008287482B2

(12) **United States Patent**
Badawi et al.

(10) **Patent No.: US 8,287,482 B2**
(45) **Date of Patent: Oct. 16, 2012**

(54) **INTRAOCULAR IMPLANTS AND METHODS AND KITS THEREFOR**

(75) Inventors: **David Y. Badawi**, Northbrook, IL (US); **Paul Badawi**, San Francisco, CA (US)

(73) Assignee: **Sight Sciences, Inc.**, San Francisco, CA (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 305 days.

(21) Appl. No.: **12/695,053**

(22) Filed: **Jan. 27, 2010**

(65) **Prior Publication Data**

US 2010/0191329 A1 Jul. 29, 2010

Related U.S. Application Data

(63) Continuation of application No. 11/475,523, filed on Jun. 26, 2006, now Pat. No. 7,909,789.

(51) **Int. Cl.**
A61M 5/00 (2006.01)
A61F 2/04 (2006.01)

(52) **U.S. Cl.** **604/8**; 604/9; 623/23.64; 623/23.7

(58) **Field of Classification Search** 604/8, 9, 604/264; 623/23.64, 23.7

See application file for complete search history.

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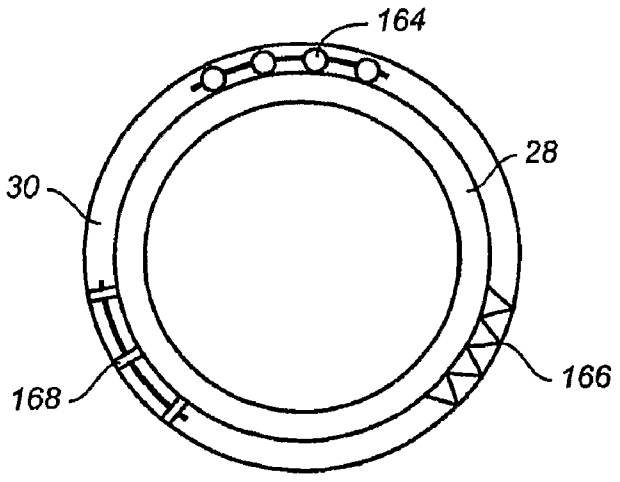
(Continued)

Primary Examiner — Leslie Deak
(74) *Attorney, Agent, or Firm* — Morrison & Foerster LLP

(57) **ABSTRACT**

Devices, methods and kits are described for reducing intraocular pressure. The devices include a support that is implantable within Schlemm's canal and maintains the patency of the canal without substantially interfering with transmural fluid flow across the canal. The devices utilize the natural drainage process of the eye and can be implanted with minimal trauma to the eye. Kits include a support and an introducer for implanting the support within Schlemm's canal. Methods include implanting a support within Schlemm's canal, wherein the support is capable of maintaining the patency of the canal without substantial interference with transmural fluid flow across the canal.

86 Claims, 15 Drawing Sheets



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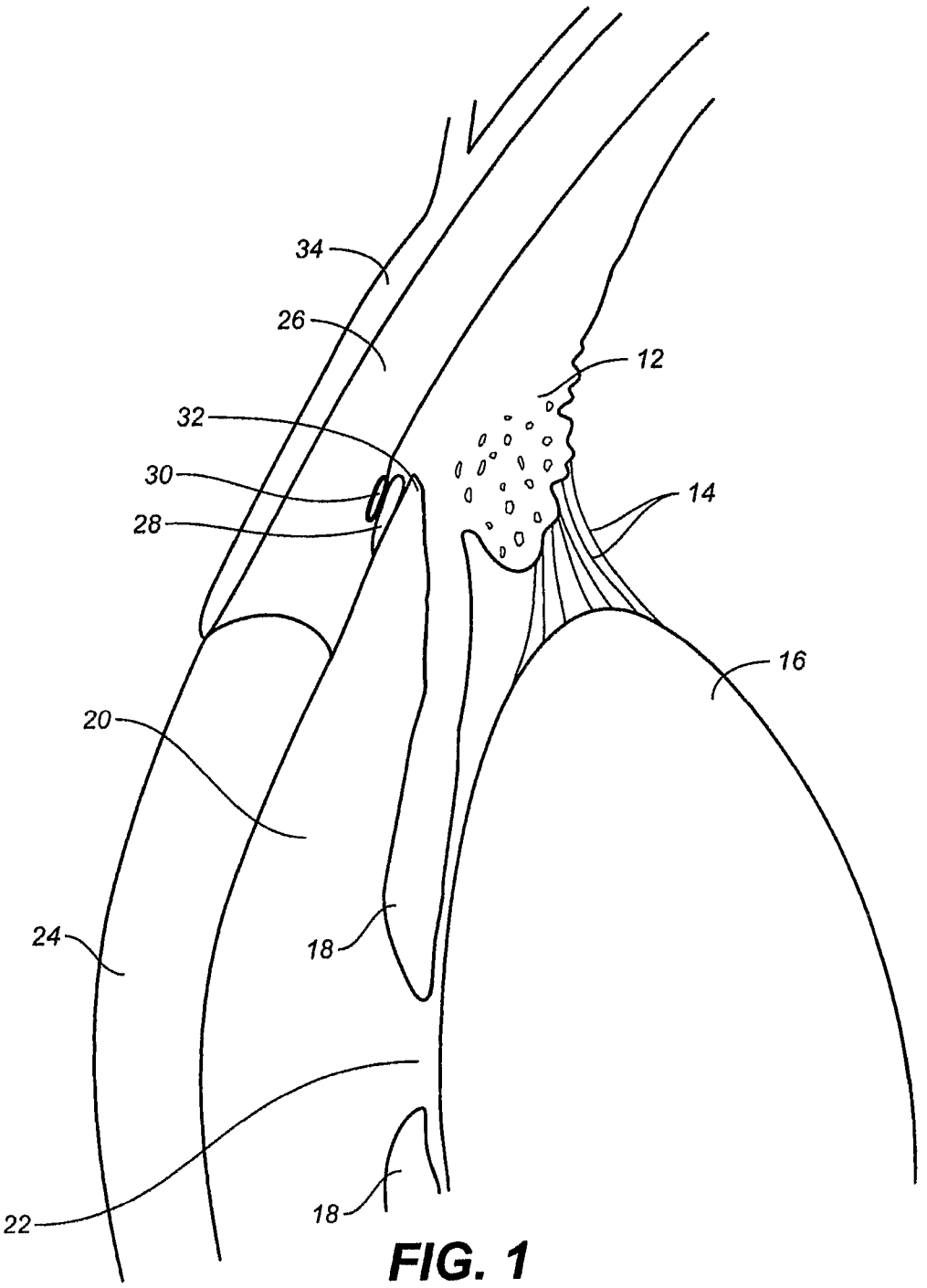

FIG. 1

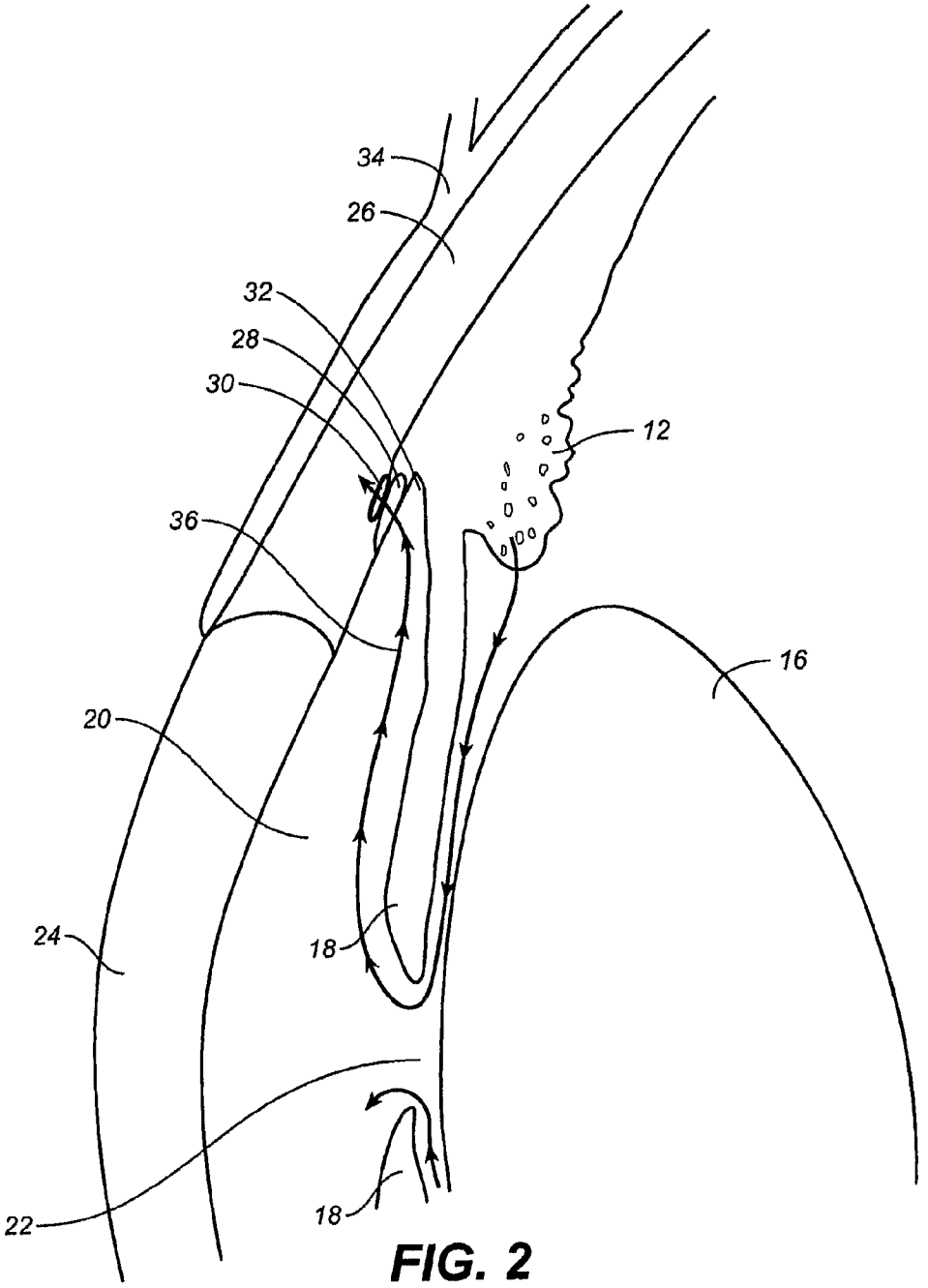

FIG. 2

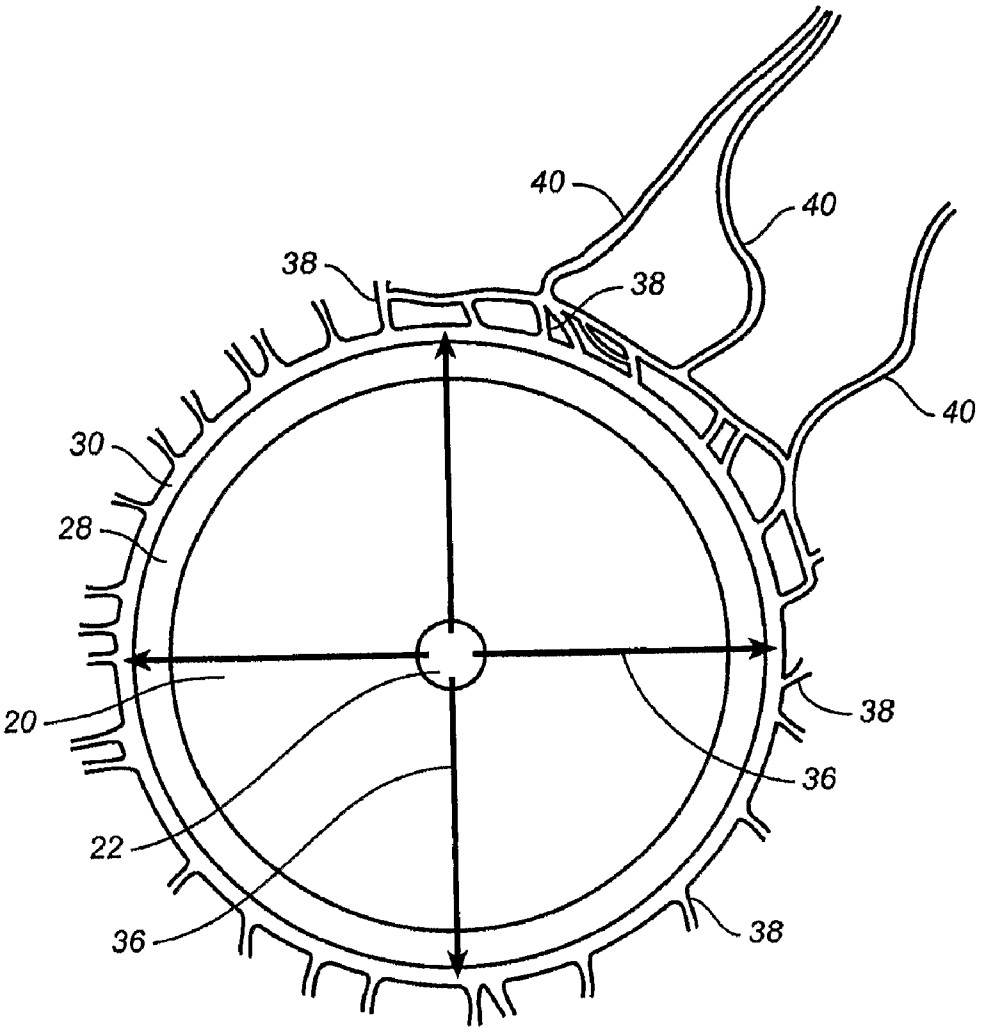

FIG. 3

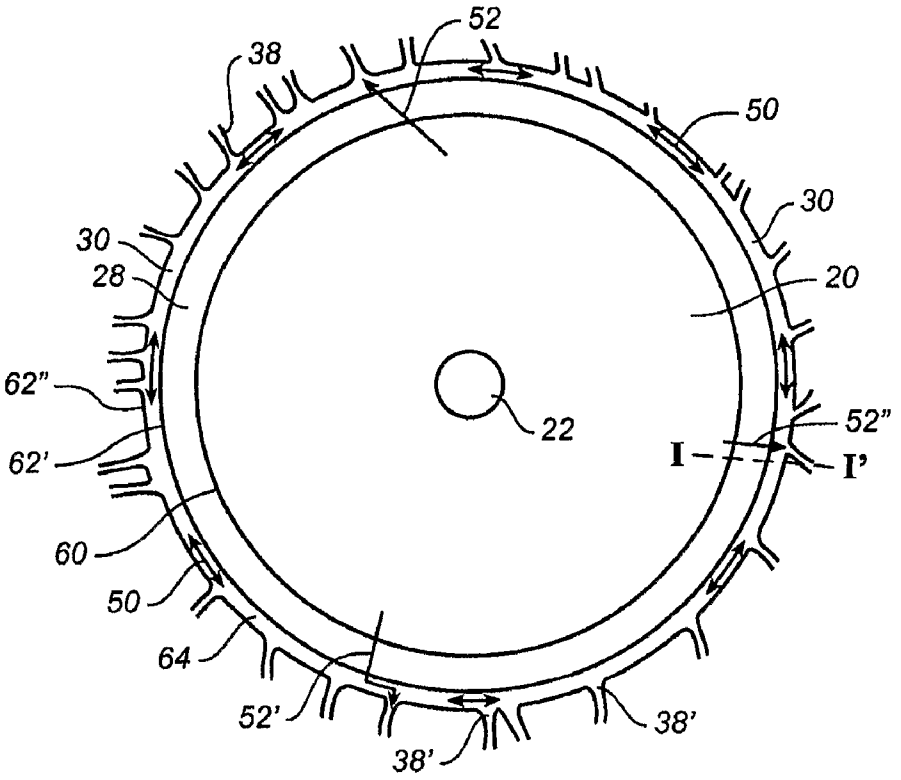
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FIG. 4A

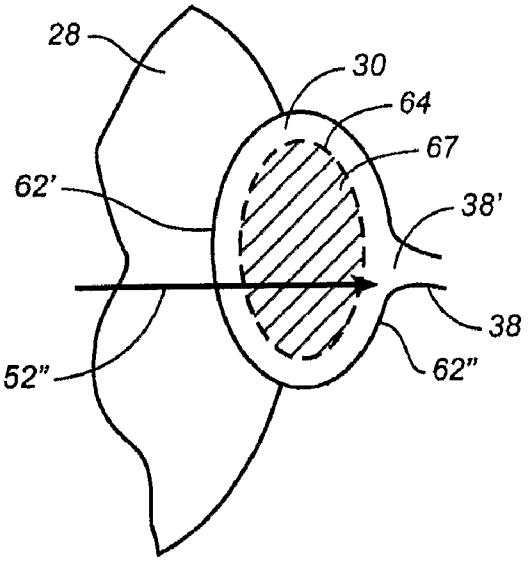
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FIG. 4B

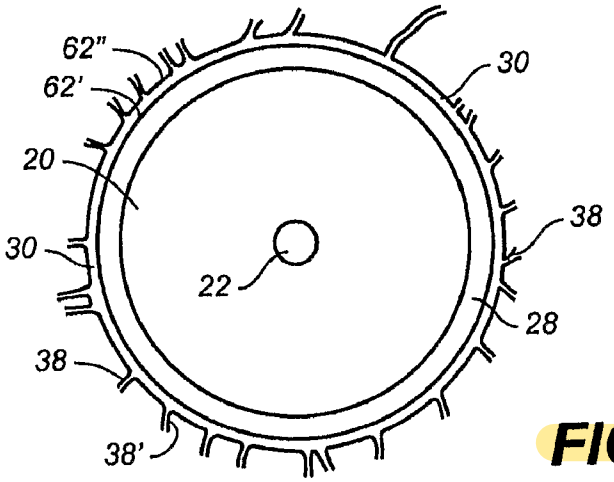


FIG. 5A

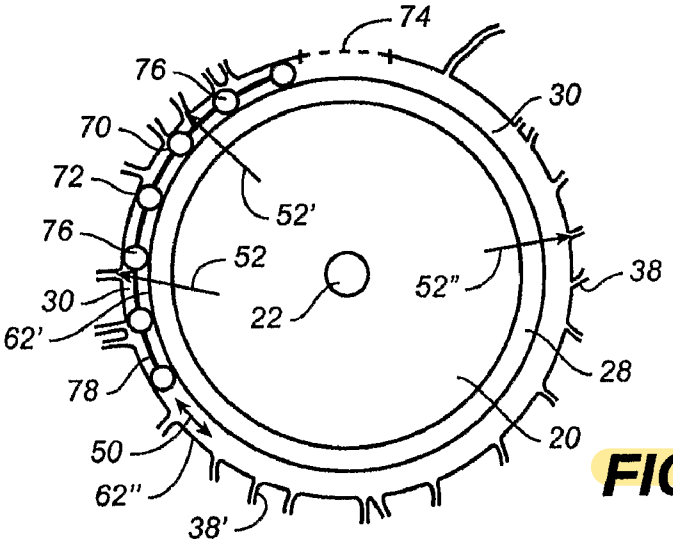


FIG. 5B

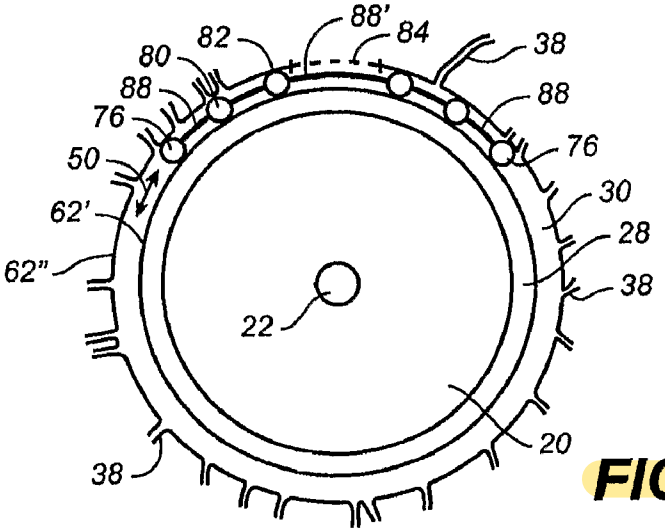


FIG. 5C

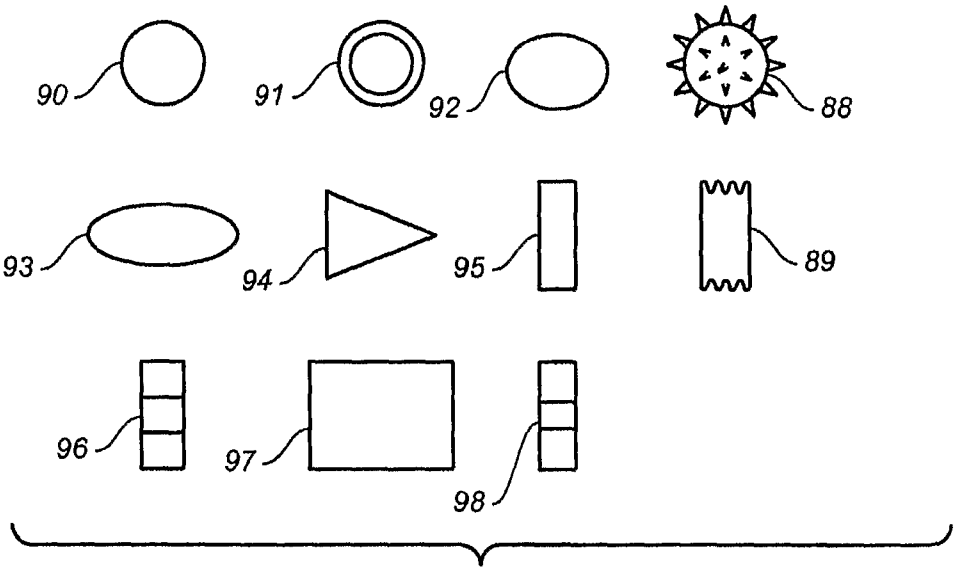


FIG. 6A

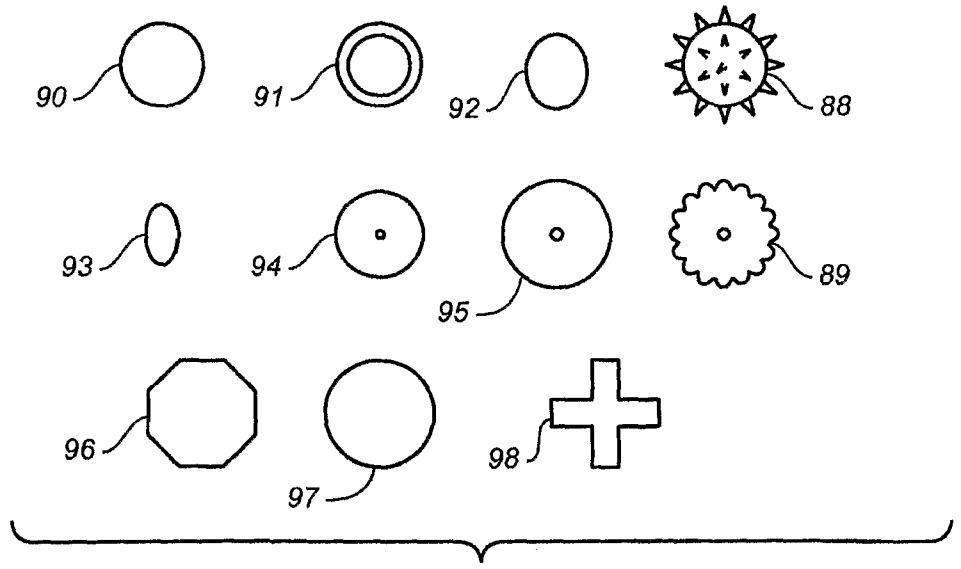


FIG. 6B

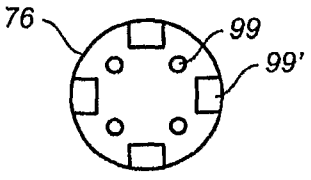


FIG. 6C

FIG. 7A

FIG. 7B

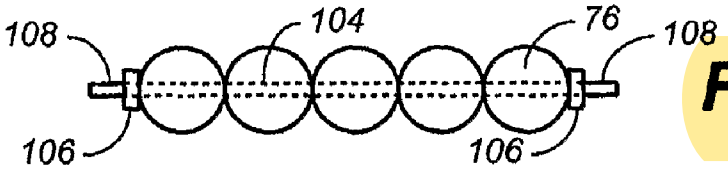


FIG. 7C

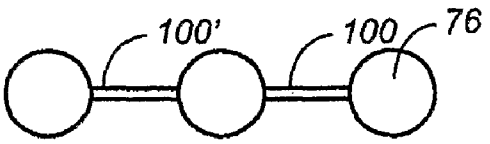


FIG. 7D

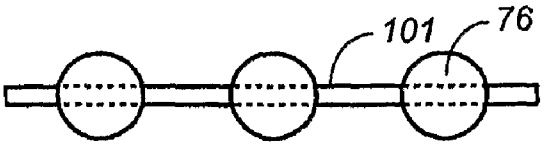


FIG. 7E

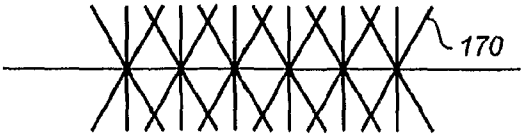


FIG. 8A

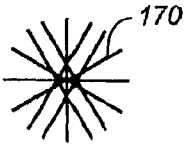


FIG. 8B

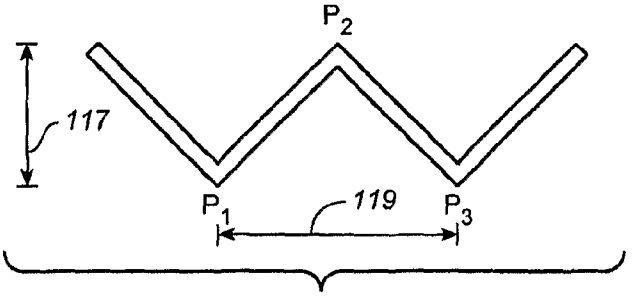


FIG. 8C

FIG. 8D

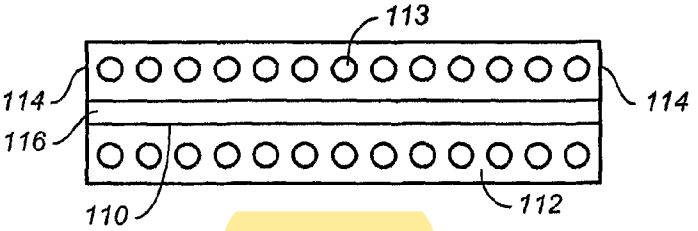


FIG. 8E

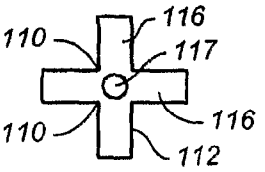


FIG. 8F

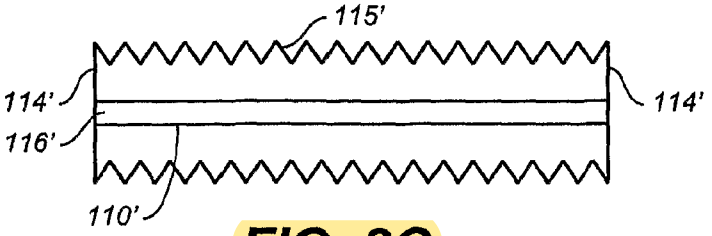


FIG. 8G

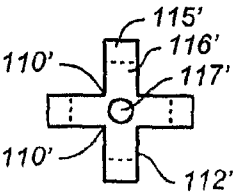


FIG. 8H

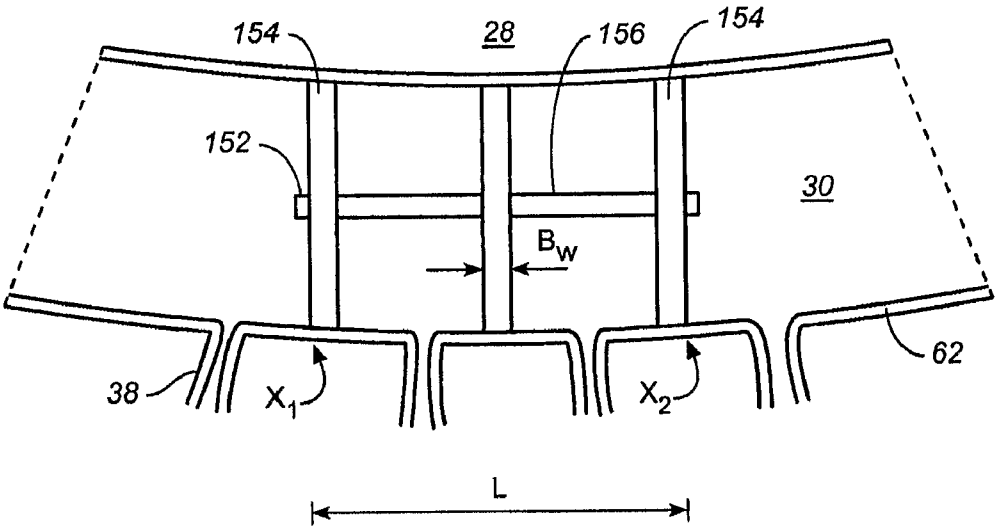
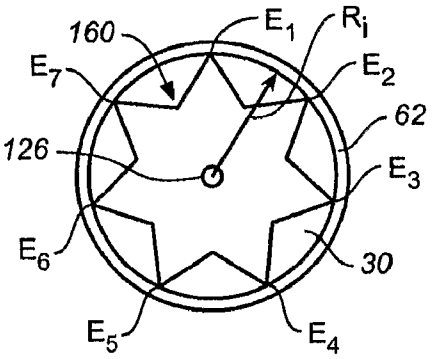

154
28
156
154
152
30
B_W
38
X_1
X_2
62
L

FIG. 9A


160
E_1
R_i
E_7
E_2
62
126
E_3
E_6
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E_5
E_4

FIG. 9B

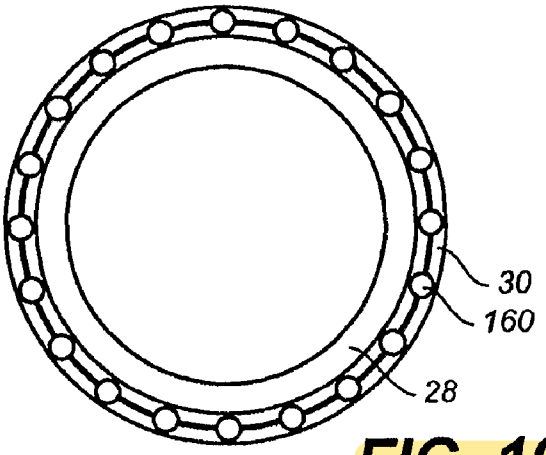

FIG. 10A

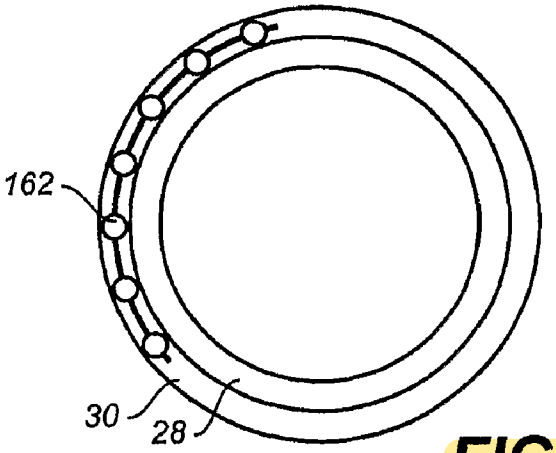

FIG. 10B

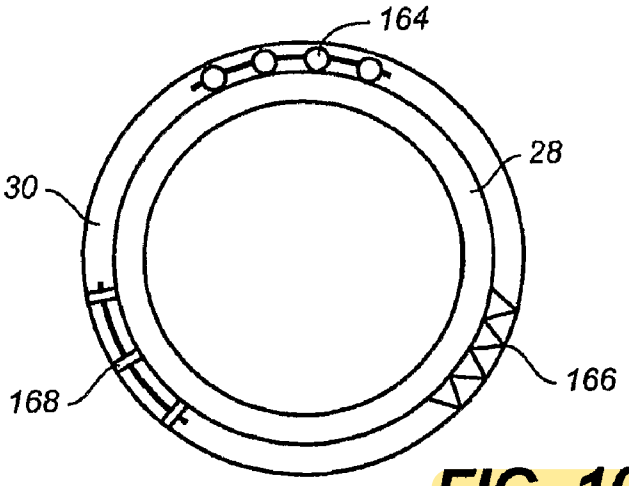

FIG. 10C

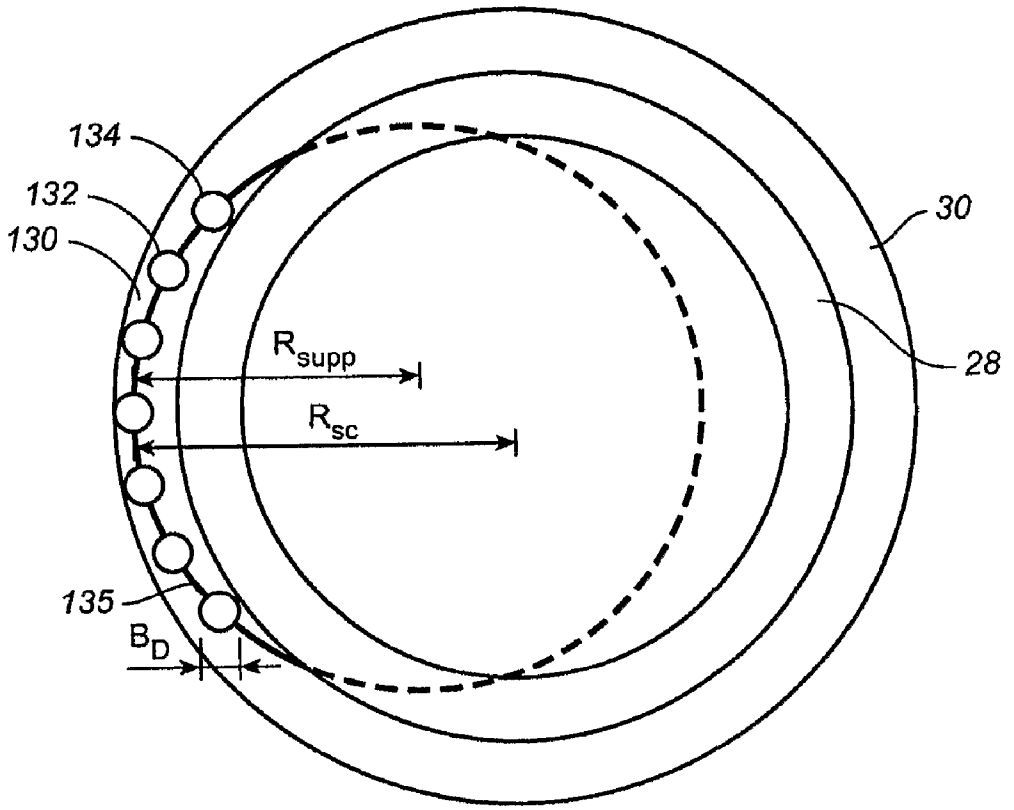

FIG. 11A

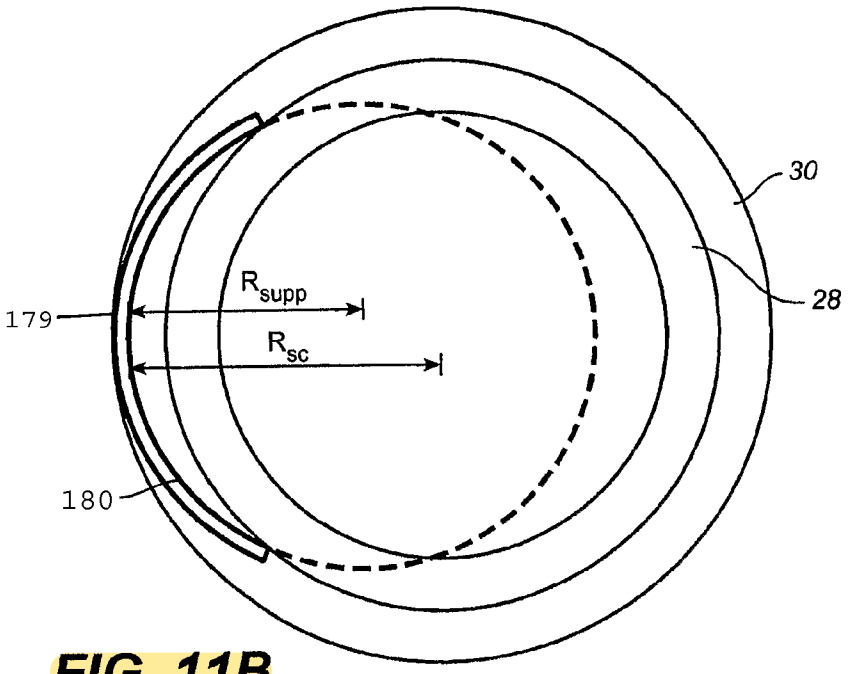

FIG. 11B

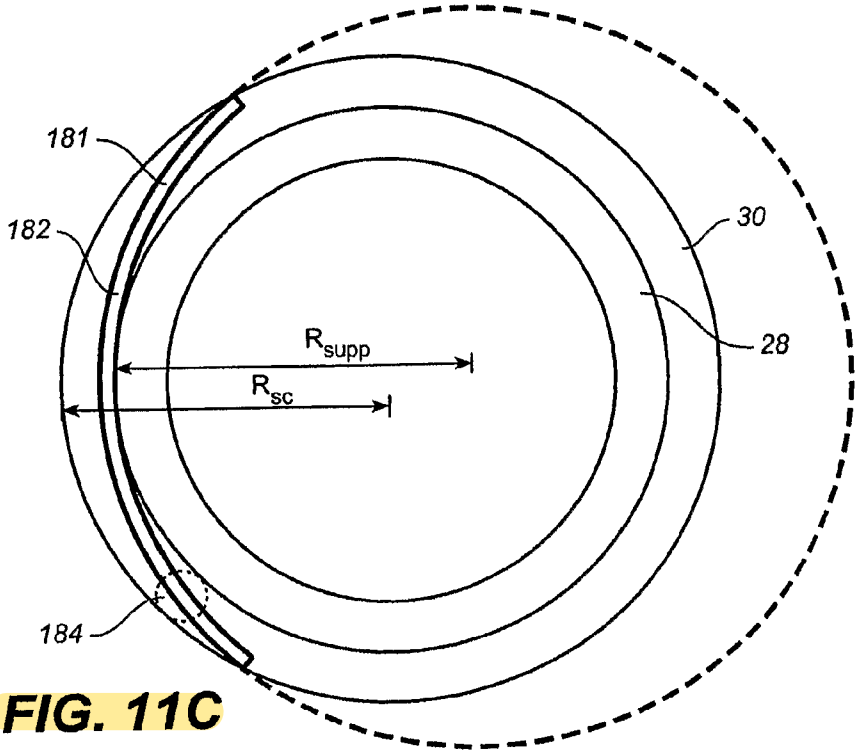

FIG. 11C

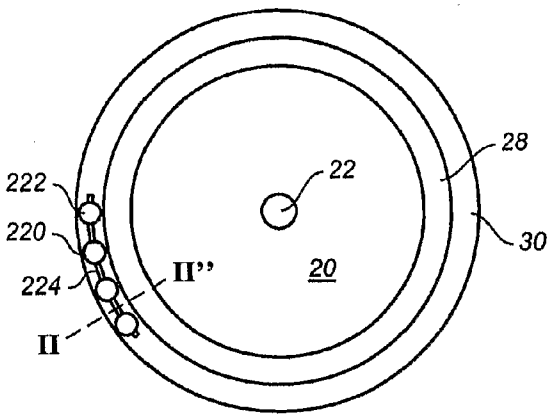

FIG. 12A

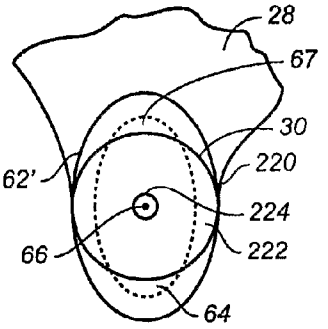

FIG. 12B

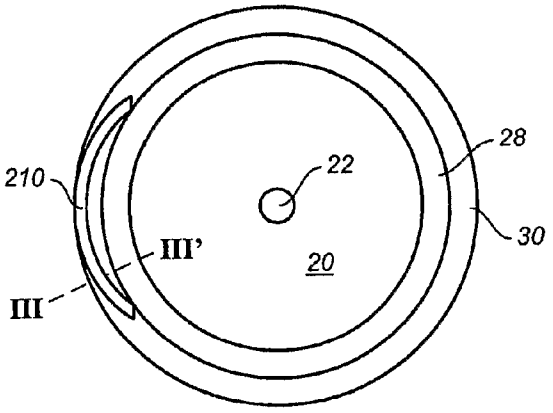

FIG. 12C

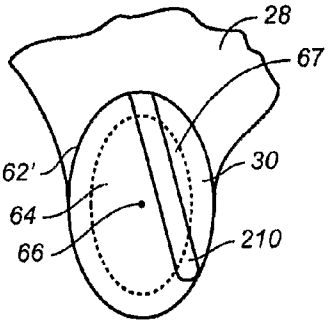

FIG. 12D

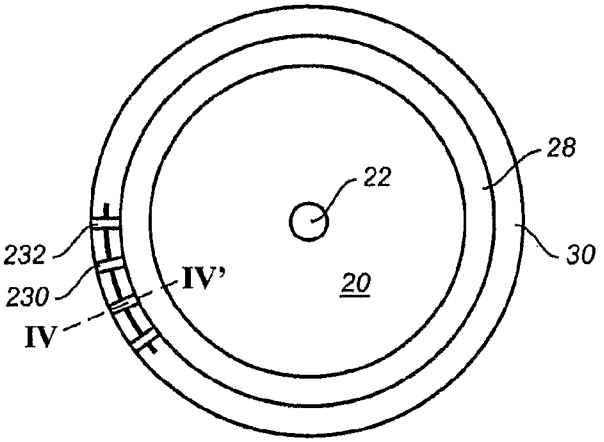

FIG. 12E

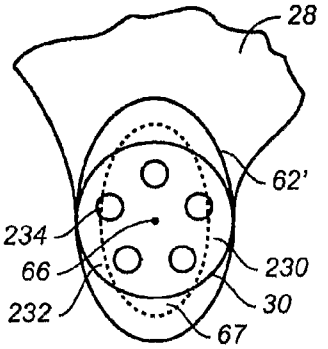

FIG. 12F

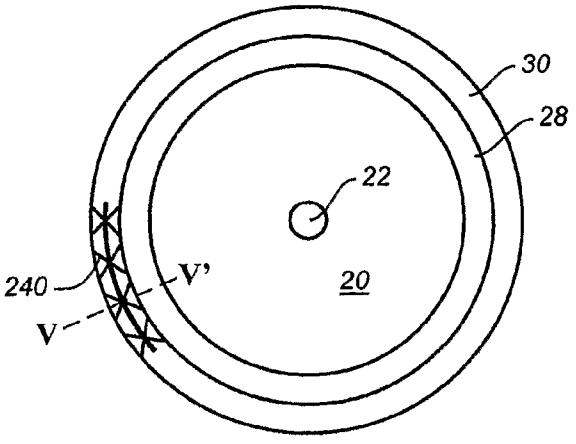

FIG. 12G

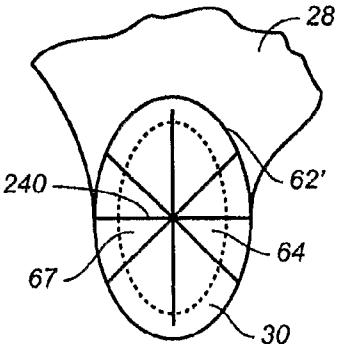

FIG. 12H

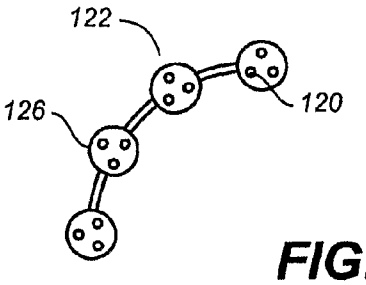

FIG. 13

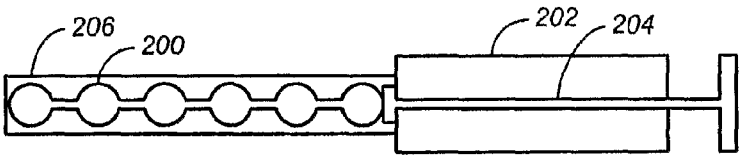

FIG. 14A

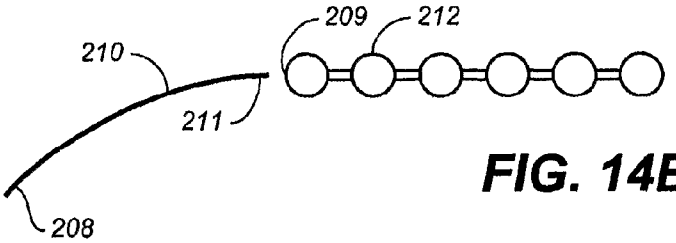

FIG. 14B

FIG. 14C

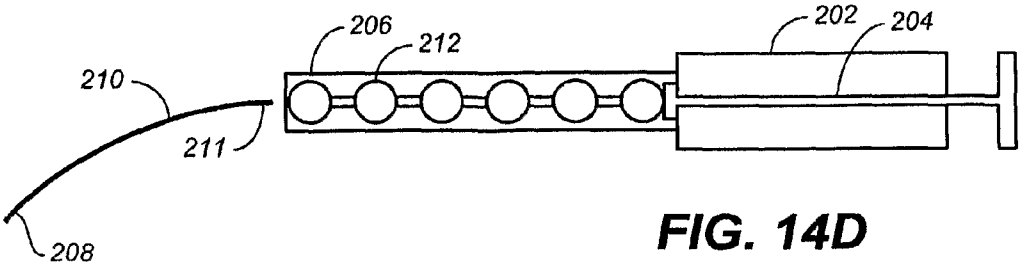

FIG. 14D

INTRAOCULAR IMPLANTS AND METHODS AND KITS THEREFOR

CROSS-REFERENCE TO RELATED APPLICATIONS

This application is a continuation of U.S. patent application Ser. No. 11/475,523, filed on Jun. 26, 2006, the disclosure of which is incorporated herein by reference in its entirety

FIELD

The devices, kits and methods described herein relate generally to intraocular pressure reduction. More particularly, the devices, kits and methods relate to intraocular implants implantable into Schlemm's canal that can reduce intraocular pressure without substantially interfering with fluid flow across Schlemm's canal.

BACKGROUND

Glaucoma is a potentially blinding disease that affects over 60 million people worldwide, or about 1-2% of the population. Typically, glaucoma is characterized by elevated intraocular pressure. Increased pressure in the eye can cause damage to the optic nerve which can lead to loss of vision if left untreated. Consistent reduction of intraocular pressure can slow down or stop progressive loss of vision associated with glaucoma. In addition, patients are often diagnosed with pre-glaucoma and ocular hypertension when they exhibit symptoms likely to lead to glaucoma, such as somewhat elevated intraocular pressure, but do not yet show indications of optic nerve damage. Treatments for glaucoma, pre-glaucoma and ocular hypertension primarily seek to reduce intraocular pressure.

Increased intraocular pressure is caused by sub-optimal efflux or drainage of fluid (aqueous humor) from the eye. Aqueous humor or fluid is a clear, colorless fluid that is continuously replenished in the eye. Aqueous humor is produced by the ciliary body, and then flows out primarily through the eye's trabecular meshwork. The trabecular meshwork extends circumferentially around the eye at the anterior chamber angle, or drainage angle, which is formed at the intersection between the peripheral iris or iris root, the anterior sclera or scleral spur and the peripheral cornea. The trabecular meshwork feeds outwardly into Schlemm's canal, a narrow circumferential passageway generally surrounding the exterior border of the trabecular meshwork. Positioned around and radially extending from Schlemm's canal are aqueous veins or collector channels that receive drained fluid. The net drainage or efflux of aqueous humor can be reduced as a result of decreased facility of outflow, decreased outflow through the trabecular meshwork and canal of Schlemm drainage apparatus, increased episcleral venous pressure, or possibly, increased production of aqueous humor. Flow out of the eye can be restricted by blockages or constriction in the trabecular meshwork and/or Schlemm's canal.

Glaucoma, pre-glaucoma and ocular hypertension currently can be treated by reducing intraocular pressure using one or more modalities, including medication, incisional surgery, laser surgery, cryosurgery, and other forms of surgery. In the United States, medications or medical therapy are typically the first lines of therapy. If medical therapy is not sufficiently effective, more invasive surgical treatments may be used. In other countries, such as those with socialized medical systems or with nationalized health care systems, surgery may be the first line of therapy if it is considered a more cost effective treatment.

A standard incisional surgical procedure to reduce intraocular pressure is trabeculectomy, or filtration surgery. This procedure involves creating a new drainage site for aqueous humor. Instead of naturally draining through the trabecular meshwork, a new drainage pathway is created by removing a portion of sclera and trabecular meshwork at the drainage angle. This creates an opening or passage between the anterior chamber and the subconjunctival space that is drained by conjunctival blood vessels and lymphatics. The new opening may be covered with sclera and/or conjunctiva to create a new reservoir called a bleb into which aqueous humor can drain. However, trabeculectomy carries both long and short term risks. These risks include blockage of the surgically-created opening through scarring or other mechanisms, hypotony or abnormally low intraocular pressure, expulsive hemorrhage, hyphema, intraocular infection or endophthalmitis, shallow anterior chamber angle, and others. Alternatives to trabeculectomy are actively being sought.

Bypass stents are also used to bridge a blocked trabecular meshwork. Stents can be inserted between the anterior chamber of the eye and Schlemm's canal, bypassing the trabecular meshwork. However, it is difficult to consistently and reliably implant a bypass stent from the anterior chamber into Schlemm's canal. The implant procedure is challenging and stents can become clogged and lose functionality over time. Others have inserted tubular elongated cylindrical hollow stents longitudinally into Schlemm's canal. Cylindrical hollow stents can be configured to allow circumferential fluid flow around the canal. These too can lose functionality over time as a result of occlusion or scarring.

Schlemm's canal is small, approximately 190-370 microns in cross-sectional diameter, and circular. Therefore, it can be difficult or expensive to design and manufacture hollow tubular stents of appropriate dimensions for use in opening Schlemm's canal. In addition, hollow tubular stents can be prone to failure and collapse or occlusion over time, as has been shown for cardiovascular stents. Hollow tubular stents incorporating thin walls are especially prone to failure. Further, the walls of tubular stents placed lengthwise along Schlemm's canal can have significant surface area contact with the trabecular meshwork and/or the collector channels, which can result in blockage of the meshwork or collector channels, substantially interfering with transmural flow across Schlemm's canal and into the eye's collector channels.

Therefore, easily manufacturable, minimally invasive devices for effective, long-term reduction in intraocular pressure are desirable. In addition, methods and kits incorporating such devices are desirable.

SUMMARY

Described here are devices, kits and methods for reducing intraocular pressure. The devices for reducing pressure within the eye comprise a support implantable circumferentially within Schlemm's canal that is configured to maintain the patency of at least a portion of the canal. The support occupies at least a portion of a central core of Schlemm's canal. The support does not substantially interfere with transmural flow across Schlemm's canal, and thereby utilizes the eye's natural drainage pathways. The support can be implanted into Schlemm's canal with minimal trauma to the eye.

The support generally comprises a biocompatible material. At least a portion of the support can be made from a biocom-

patible polymer, e.g., acrylics, silicones, polymethylmethacrylate, or a hydrogel. In addition, at least part of the support can be made from a biocompatible metal such as gold. In some variations, at least a portion of the support is made from a shape memory material. Suitable shape memory materials include shape memory polymers or shape memory alloys, such as nickel titanium alloys. If a shape memory material is used, the support can have a compressed state prior to and during implantation into Schlemm's canal, and an expanded state following implantation to open the canal.

In some variations, the support is at least partially made from a biocompatible, biodegradable polymer. The biodegradable polymer can be collagen, a collagen derivative, a poly(lactide); a poly(glycolide); a poly(lactide-co-glycolide); a poly(lactic acid); a poly(glycolic acid); a poly(lactic acid-co-glycolic acid); a poly(lactide)/poly(ethylene glycol) copolymer; a poly(glycolide)/poly(ethylene glycol) copolymer; a poly(lactide-co-glycolide)/poly(ethylene glycol) copolymer; a poly(lactic acid)/poly(ethylene glycol) copolymer; a poly(glycolic acid)/poly(ethylene glycol) copolymer; a poly(lactic acid-co-glycolic acid)/poly(ethylene glycol) copolymer; a poly(caprolactone); a poly(caprolactone)/poly(ethylene glycol) copolymer; a polyorthoester; a poly(phosphazene); a poly(hydroxybutyrate) or a copolymer including a poly(hydroxybutyrate); a poly(lactide-co-caprolactone); a polycarbonate; a poly(esteramide); a polyanhydride; a poly(dioxanone); a poly(alkylene alkylate); a copolymer of polyethylene glycol and a polyorthoester; a biodegradable polyurethane; a poly(amino acid); a polyetherester; a polyacetal; a polycyanoacrylate; a poly(oxyethylene)/poly(oxypropylene) copolymer; and blends and copolymers thereof.

The support can comprise an active agent. For example, a support can be coated or impregnated with an active agent. Alternatively, an active agent can be dispersed within the support, e.g., by filling a cavity within the support. The active agent can include a prostaglandin, a prostaglandin analog, a beta blocker, an alpha-2 agonist, a calcium channel blocker, a carbonic anhydrase inhibitor, a growth factor, an anti-metabolite, a chemotherapeutic agent, a steroid, an antagonist of a growth factor, or combinations thereof. The release of the active agent can be controlled using a time release system, e.g., by embedding or encapsulating the active agent with a time release composition.

In some variations, the support will be solid. In other variations, at least a portion of the support will be hollow or porous. The surface of the support may be smooth, rough, spiked, or fluted. In still other variations, at least part of the support will be made from mesh. The support can include at least one fenestration and one or more rod-like members.

In some variations, the support comprises at least two adjacent beads. Adjacent beads can have the same or different sizes and shapes, and can be made from the same or different materials. The bead shapes can be spherical, spheroid, ovoid, cylindrical, cuboid, cubical, conical, discoid, helical, or segments thereof. In some variations, there is a connector linking at least two adjacent beads together. If there is a connector, it can be rigid or flexible. If there is more than one connector, e.g., two connectors inserted between three beads, the connectors may be of the same or different lengths. The connectors can include the same or different material as the beads they connect. A connector can also function as a spacer configured to provide space between adjacent beads. In some variations, the support comprises at least two discs separated by, and connected with, a connector. The discs may include fenestrations. The connector may also comprise a guide wire over which a fenestrated bead can be threaded into the canal of Schlemm.

The support can extend approximately all the way around Schlemm's canal, if the support has a circumference approximately equal to the circumference of Schlemm's canal. Alternatively, the support can extend only about half way around the circumference of Schlemm's canal, or about a quarter way around the canal. In some variations, the support will extend less than a quarter circumference of Schlemm's canal. The support can be configured to contact the inner surface of the wall of Schlemm's canal at two, three or more points. In some variations, the support can be attached to tissue. The support may comprise a stiff arcuate member having a radius of curvature smaller or larger than that of Schlemm's canal.

In some variations, the support can be altered using electromagnetic radiation. For example, a laser having a wavelength absorbable by at least one localized portion of the support can be used to alter the support. In other variations, electromagnetic radiation can be used to release an active agent from the support. In still other variations, the support can be visually enhanced using fluorescence or phosphorescence emission. For example, the support can comprise a chromophore that fluoresces or phosphoresces upon excitation with a light source. In some variations, the emitted fluorescence or phosphorescence is in the wavelength range of about 300 nm to about 800 nm. In some variations, the support can comprise a chromophore that enhances postoperative monitoring of the support.

Kits for reducing intraocular pressure are also provided. The kits contain a support that can be implanted circumferentially within Schlemm's canal. The support is configured to maintain the patency of at least part of Schlemm's canal. The support occupies at least a portion of a central core of Schlemm's canal and does not substantially interfere with transmural flow across the canal. The kits also contain an introducer for implanting the support within the canal. In some variations, the kits include a positioning device for adjusting the support within the canal. In other variations, kits include instructions. In still other variations, the kits include an active agent. Some kits contain at least two supports. If more than one support is included, the kits can include at least two introducers for delivering the supports. Multiple supports within the same kit can have the same or different shape, size, or composition. Multiple supports within the same kit can be connected together or remain separate. In some variations, kits include a fixation device for attaching a support to tissue. In other variations, kits may include a system for visually enhancing the appearance of the support.

Methods for reducing intraocular pressure are also described. The methods include inserting a support circumferentially within Schlemm's canal. The support is configured to maintain the patency of at least part of the canal. The support occupies at least a portion of a central core of Schlemm's canal, and does not substantially interfere with transmural flow across the canal. In some variations, the methods also include dilating Schlemm's canal prior to insertion of the support. In still other variations, the methods comprise anchoring the support to tissue. The methods can include implanting at least two supports. If more than one support is implanted within a single eye, the multiple supports can be positioned circumferentially adjacent to each other or circumferentially opposed (i.e., positioned about 180° apart) to each other within Schlemm's canal. Multiple supports within one eye can be connected or remain separate. In some variations of the methods, the support is illuminated with a light source to visually enhance the position of the support. In

other variations of the methods, the support can be altered using electromagnetic radiation. For example, a laser absorbed by at least one localized portion of the support can be used to alter the support. The alteration can comprise the creation or enlargement of an aperture in the support. If electromagnetic radiation is used to alter a support, the alteration can occur before implantation or after implantation.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. **1** provides a partial cross-sectional side view of a normal human eye.

FIG. **2** provides a partial cross-sectional side view of a normal drainage path of fluid from the eye.

FIG. **3** shows a front view of normal fluid drainage from the eye.

FIG. **4**A shows an alternative front view of normal fluid drainage paths from the eye. FIG. **4**B shows a cross-sectional view along line I-I'.

FIG. **5**A provides a front view of an eye in which Schlemm's canal is narrowed or collapsed. FIG. **5**B shows a front view of a device including a support inserted into Schlemm's canal that allows transmural flow across the canal. FIG. **5**C illustrates an alternate design for a device inserted into Schlemm's canal that allows transmural flow across the canal.

FIG. **6**A shows side views of various element or bead configurations that can be used in the supports described herein. FIG. **6**B shows the corresponding front views of the element or bead configurations shown in FIG. **6**A. FIG. **6**C illustrates an element or bead having fenestrations.

FIG. **7**A illustrates a support having multiple juxtaposed beads. FIG. **7**B illustrates a support having multiple juxtaposed and connected beads. FIG. **7**C shows an alternate configuration of a support having multiple juxtaposed and connected beads. FIG. **7**D shows a support having multiple, spaced-apart but connected beads. FIG. **7**E illustrates beads threaded onto a connector.

FIGS. **8**A-B show side and front views, respectively, of a support having an open network structure. FIGS. **8**C-D show side and front views, respectively, of a support having a longitudinal zig-zag configuration that will contact the wall of Schlemm's canal at least three points (labeled P_1, P_2, P_3). FIGS. **8**E-F show side and front views, respectively, of a support having a rod-like member with continuously fluted edges and fenestrations. FIGS. **8**G-H show side and front views, respectively, of another variation of a support having a rod-like member with continuously fluted edges.

FIGS. **9**A-B show expanded cross-sectional views of a support implanted within Schlemm's canal.

FIGS. **10**A-C illustrate various configurations of supports implanted into Schlemm's canal.

FIGS. **11**A-B illustrate two configurations of supports having a smaller radius of curvature than Schlemm's canal. FIG. **11**C shows a support having a larger radius of curvature than Schlemm's canal.

FIG. **12**A illustrates a variation of a support traversing the center of the central core of Schlemm's canal. FIG. **12**B shows a cross-sectional view along line II-II'. FIG. **12**C illustrates a variation of a support traversing the central core of the canal. FIG. **12**D shows a cross-sectional view along line III-III'. FIG. **12**E illustrates a variation of a support that occupies the majority of the central core of the canal. FIG. **12**F shows a cross-sectional view along line IV-IV'. FIG. **12**G illustrates a variation of support having an open network that occupies a portion of the central core of the canal. FIG. **12**H shows a cross-sectional view along line V-V'.

FIG. **13** shows an illustrative example of a support that can be modified using electromagnetic radiation.

FIG. **14**A illustrates a syringe that can be used to insert a support into Schlemm's canal. FIG. **14**B illustrates a variation in which a support is threaded onto a guide element for insertion and positioning in Schlemm's canal. FIG. **14**C illustrates a cross-sectional view of a support having a central bore to accommodate a guide element. FIG. **14**D illustrates a variation in which a syringe and a guide element are used for insertion and positioning of a support in Schlemm's canal.

DETAILED DESCRIPTION

Described here are devices, kits and methods to reduce intraocular pressure by maintaining or restoring Schlemm's canal so that at least a portion of the canal is patent or unobstructed. The devices, kits and methods operate to keep Schlemm's canal from collapsing while not substantially interfering with the eye's natural drainage mechanism for aqueous humor, in which transmural fluid flow across Schlemm's canal occurs. The devices are implantable in Schlemm's canal with minimal trauma to the eye.

With reference to the figures, FIG. **1** shows a partial cross-sectional view of the anatomy of a normal human eye. Ciliary body **12** is connected to iris **18** and to lens **16** via zonular fibrils **14**. The anterior chamber of the eye **20** is bounded on its anterior (front) surface by cornea **24**. In the center of iris **18** is pupil **22**. Cornea **24** is connected on its periphery to sclera **26**, which is a tough fibrous tissue forming the white shell of the eye. Trabecular meshwork **28** is located on the outer peripheral surface of anterior chamber **20**. The trabecular meshwork extends 360° circumferentially around the anterior chamber. Located on the outer peripheral surface of meshwork **28** is Schlemm's canal **30**. Schlemm's canal extends 360° circumferentially around the trabecular meshwork. At the apex formed between iris **18**, meshwork **28** and sclera **26** is angle **32**. Conjunctiva **34** is a membrane overlaying sclera **26** and lining the inside of the eyelid (not shown).

FIG. **2** shows a partial cross-sectional view of flow of aqueous humor within and out of a normally functioning human eye. Aqueous humor is produced in ciliary body **12** and its path through and out of the eye is indicated by solid directional line **36**. The aqueous humor flows from ciliary body **12**, between lens **16** and iris **18**, through pupil **22** into anterior chamber **20**, across trabecular meshwork **28**, across Schlemm's canal **30**, into aqueous veins or collector channels (not shown) and finally into the bloodstream via conjunctival vasculature.

FIG. **3** shows a front view of normal flow of aqueous humor out of the eye. Aqueous humor enters anterior chamber **20** via pupil **22**. The fluid flows outwardly toward the periphery of the eye, with the general path of flow indicated by solid directional lines **36**. The fluid crosses trabecular meshwork **28** and traverses Schlemm's canal **30** to reach aqueous veins or collector channels **38**. There are typically 25-30 collector channels located in a human eye. Collector channels **38** are connected to vasculature **40**, whereby the drained aqueous humor enters the bloodstream. Although the direction of net or bulk fluid flow is depicted as radially outward by directional lines **36** from pupil **22** for simplicity, actual fluid flow in an eye may follow more varied paths.

Different fluid flow paths in and across Schlemm's canal are illustrated in FIGS. **4**A-B. FIG. **4**A shows a front view of an eye, and FIG. **4**B shows an expanded cross-sectional view along line I-I'. Circumferential (i.e., longitudinal) flow along and around circular canal **30** is depicted by directional lines **50**. Fluid that does not traverse canal **30** to reach collector

channels **38** may not be effectively drained from the eye. Examples of fluid flow paths that can effectively drain the eye are illustrated by directional lines **52**, **52'**, and **52"**. In each of these paths, fluid enters trabecular meshwork **28** along its inner peripheral surface **60** and exits the meshwork along its outer peripheral surface **62'**. Meshwork outer peripheral surface **62'** provides the inner peripheral surface or wall of Schlemm's canal **30**. Transmural fluid flow across Schlemm's canal involves two instances of transmural flow across walls or boundaries. First, fluid must flow from trabecular meshwork **38** through inner peripheral surface or wall **62'** of Schlemm's canal **30** to reach lumen **64** of the canal. Second, fluid must flow from lumen **64** through canal outer peripheral wall **62"** through apertures **38'** to enter collector channels **38**. Finally, the collector channels **38** feed the drained fluid into vasculature. Lumen **64** of canal **30** includes a central core region **67**. Thus, fluid flow from the eye differs from fluid flow in other vessels in the body where fluid need only flow longitudinally along the vessel, such as blood flowing through a vein.

Devices

Devices to reduce intraocular pressure comprising a support that can be implanted circumferentially in Schlemm's canal to maintain the patency of at least a portion of the canal are described here. The support occupies at least a portion of a central core of Schlemm's canal and does not substantially interfere with transmural flow across the canal. By "maintain the patency" of at least a portion the canal, it is meant that the support operates to keep the canal at least partially unobstructed to transmural flow, such that fluid can 1) exit through the trabecular meshwork; 2) traverse the canal; and 3) drain via the collector channels. To maintain the patency of the canal, it is not necessary that the support leave the canal unobstructed in regard to circumferential flow. By "does not substantially interfere" with transmural flow, it is meant that the support does not significantly block either fluid outflow from the trabecular meshwork or fluid outflow to the collector channels. In many variations, the support allows between about 0.1 and about 5 microliters per minute aqueous outflux from the eye through the trabecular meshwork and collector channels. The "central core of Schlemm's canal" refers to the region around the cross-sectional center of the canal in the interior space of the canal lumen, i.e., not on the periphery of the canal. Therefore, a device that occupies at least a portion of a central core of Schlemm's canal can traverse at least a portion of the canal's lumen.

Therefore, devices described here need not comprise an open-ended tubular support placed longitudinally along Schlemm's canal, i.e., the devices and supports can be non-tubular. A longitudinal, open-ended tubular support can enable longitudinal flow along the canal. However, even if fluid can flow longitudinally (i.e., circumferentially) along Schlemm's canal, the eye may not be effectively drained unless the fluid eventually traverses the canal. That is, transmural fluid flow across two boundaries must occur: 1) fluid must flow from the trabecular meshwork through a canal inner wall coincident with an outer peripheral boundary of the trabecular meshwork to reach the canal lumen; and 2) fluid must flow from the canal lumen through apertures in the canal outer peripheral wall to reach the connector channels. The collector channels are then able to further disperse the fluid and complete the natural draining process. A tubular support inserted longitudinally into the canal can have significant surface area overlap with surfaces of the canal such that transmural flow across the canal may be significantly impeded. A longitudinal tubular support placed in Schlemm's canal may block flow into the canal from the trabecular meshwork and block flow out of the canal into the collector channels.

Devices described herein for treating elevated intraocular pressure include a support that is implanted within Schlemm's canal. In many instances, the device will reduce the intraocular pressure by 1-40 mm Hg, for example by at least 2 mm Hg. In other instances, the device will reduce intraocular pressure by at least 4 mm Hg, or at least 6 mm Hg, or at least 10 or 20 mm Hg. In still other instances, the device will operate to bring the intraocular pressure into the range of about 8 to about 22 mm Hg. The support can be configured in a variety of ways to at least partially prop open Schlemm's canal thereby maintaining its patency without substantially interfering with or impeding transmural fluid flow across Schlemm's canal. In some variations, the support may interfere with or block longitudinal flow along or around the canal. In many instances, the support will be contained entirely within Schlemm's canal. In some variations the support will be implanted within the canal, but may extend partially beyond Schlemm's canal, e.g., into the trabecular meshwork.

In some variations, a support to maintain at least partial patency for Schlemm's canal to enable fluid flow between an inner wall of the canal and an outer wall of the canal can comprise elements or structures such as bead-like elements or beads, which can be connected together, e.g., as a string of beads. Individual elements or beads or a connected group of elements or beads can be inserted directly into Schlemm's canal. A more detailed description of supports incorporating elements or beads is provided below.

FIG. **5**A illustrates a front view of an eye having a narrowed or collapsed Schlemm's canal **30**, where canal outer peripheral wall **62"** is very close to canal inner peripheral wall **62'**. Although Schlemm's canal **30** is depicted in FIG. **5**A as being uniformly narrow around the entire circumference of canal, it is possible that only a portion of Schlemm's canal is narrowed or collapsed. When Schlemm's canal is collapsed or narrowed, net efflux of aqueous from the anterior chamber to the collector channels **38** is diminished, thereby increasing intraocular pressure. As a result, the risk of pre-glaucoma, ocular hypertension, or glaucoma can increase.

FIG. **5**B illustrates an example of a device **70** inserted into Schlemm's canal **30** through incision site **74**. Device **70** in this example is positioned to one side of incision site **74**. Device **70** includes support **72** that is configured to keep Schlemm's canal at least partially open to transmural fluid flow across both canal inner wall **62'** and canal outer wall **62"** to reach collector channels **38** via apertures **38'**. In the example shown in FIG. **5**B, support **72** includes elements or beads **76** connected with connectors **78**. In this variation, the distance between canal inner wall **62'** and outer wall **62"** is approximately determined by the cross-sectional dimension of support **72**, which is in turn determined by the largest cross-sectional diameter of the beads **76**. Therefore, circumferential (i.e., longitudinal) fluid flow around and along the canal **30** indicated by directional line **50** may be inhibited by the insertion of support **72** into the canal. However, transmural flow across both walls or boundaries of the canal indicated by directional lines **52**, **52'**, **52"** is enhanced by support **72** and fluid is able to reach collector channels **38** and be drained from the eye. As a result, support **72** can effectively reduce intraocular pressure by utilizing the eye's natural drainage mechanism. Incision **74** need only be large enough to accommodate the diameter of beads **76**, so that trauma to the eye is minimized. Beads can have cross-sectional dimensions in the range from about 50 microns to about 500 microns. Insertion of beads having relatively small cross-sectional diameters

(e.g., about 50 microns) into Schlemm's canal open the canal less than the normal cross-sectional diameter of the canal, which is about 190 to about 370 microns, but still can maintain the patency of the canal. Insertion of beads having relatively large cross-sectional diameters (e.g., greater than about 300 microns) can open the canal as large as or larger than the canal's normal cross-sectional diameter and also can operate to stretch the trabecular meshwork. Stretching the trabecular meshwork may further enhance drainage.

FIG. **5**C illustrates an alternate configuration of a device **80** inserted into Schlemm's canal **30** through incision site **84**. Device **80** includes support **82** that extends to both sides of incision site **84**. Support **82** includes elements or beads **76** connected with connectors **88** and **88'**. In this example, connector **88'** is of a different length than connectors **88**. As in FIG. **5**B, beads **76** may impede circumferential (i.e., longitudinal) fluid flow around and along canal **30** indicated by directional line **50**. However transmural flow across the canal is enhanced by support **82** that maintains patency across the canal and allows fluid to reach collector channels **38**. If the beads are fenestrated or comprise rough, spiked, or fluted perimeters, then circumferential fluid flow through or around the beads may also occur.

Elements or beads used in a support may be hollow and closed structures, open structures, solid structures, porous structures, or any combination thereof, and may be of any suitable shape. FIGS. **6**A and **6**B illustrate side and front views, respectively, of exemplary elements or beads that may be used in the supports described here. As shown, solid **90** or hollow **91**, spherical **90**, spheroid **92**, ovoid **93**, conical **94**, disk-shaped **95**, polyhedral **96**, rod-like **97**, or beads with fluted edges **98**, rough edges, **89**, or spiked edges **88** may be used. In some instances, it may be desired to round corners or edges of the beads. As illustrated in FIG. **6**C, elements or beads **76** may include fenestrations **99**, **99'**. Fenestrations may have any suitable cross-sectional shape, such as round or quadrilateral. Although a disc-shaped bead **76** is shown in FIG. **6**C, any shape of bead can be fenestrated.

As illustrated in the variations shown in FIGS. **7**A-E, two or more beads **76** in a support may be adjacent to each other. Adjacent beads may be juxtaposed (FIG. **7**A), connected and juxtaposed (FIGS. **7**B and **7**C), or connected together with connectors **100**, **100'** to form intervals between beads (FIG. **7**D). In addition, beads may be threaded onto a connector **101** (FIG. **7**E). Multiple beads used in a single support may have the same or different shapes, and may be made of the same or different materials.

Junctions **102** between beads as shown in FIG. **7**B can be made using any suitable technique, such as by using an adhesive, chemical bonding, mechanical interlocking, or welding. Beads may also be juxtaposed and connected as shown in FIG. **7**C by threading onto a guide element **104**. Guide element **104** can comprise a fiber, a suture, a guide wire, a fixture, or the like. The beads can be fixed in a juxtaposed configuration on a guide element, e.g., by knotting ends of the fiber or by providing other end-blocking devices **106**, such as clips, caps, protrusions, or the like on ends **108** of element **104**. Any or all of the beads can be attached to guide element **104**, e.g., beads occupying end positions may be attached to element **104** and function as blocking beads to keep beads from sliding off ends **108** of element **104**. Alternatively, beads may slide along element **104**. Guide element **104** can be flexible, such as thin polymer threads, such as a suture, or metal wires. Alternatively, element **104** can be flexible but fixable, such as one or more shapeable metal wires that can be bent into a desired position and maintain that position against some amount of external stress or pressure. In other variations, guide element **104** can be rigid, e.g., a molded polymeric piece or a stiff metal piece.

As shown in FIG. **7**D, multiple connectors **100**, **100'** may be used in a single support, with at least one connector inserted between adjacent beads **76**. If multiple connectors are used, they may be of the same or different lengths. In addition, multiple connectors within the same support may be made of the same or different materials, and the connectors may be made of the same or different materials than the beads. Discrete connectors **100**, **100'** can be inserted between beads **76** and attached to adjacent beads using any suitable method including using adhesives, chemical bonding, welding, mechanical interlocking, knots, or any combination thereof. In some variations, connectors **100**, **100'** between beads can be configured to function as spacers between individual beads. As illustrated in FIG. **7**E, beads **76** can also be threaded onto a connector **101**. If the beads are threaded onto a connector, the beads can be maintained in fixed positions along the connector **101** by any suitable method, including using adhesives, chemical bonding, welding, clips, protrusions on the connector, mechanical interlocking locking between a connector and a bead, knots, or any combination thereof. Alternatively, some or all beads may slide along connector **101**. Connectors **100**, **100'**, **101** can be flexible, such as thin polymer threads or metal wires. Connectors **100**, **100'**, **101** can also be flexible but fixable, such as shapeable metal wires. Alternatively, connectors **100**, **100'**, **101** may be rigid, such as molded polymeric connectors or stiff metal connectors.

Supports of the devices described here need not contain beads. For example, a support can be a unitary structure of fixed or variable length. Supports can be solid, hollow, or porous, or any combination thereof. For example, a support can be partially solid and partially hollow. Examples of support configurations are shown in side view and front view in FIGS. **8**A-F. As illustrated in FIG. **8**A-B, a support can have an open network structure. Such a support can be fabricated out of shapeable metal wires, for example. The support illustrated in FIGS. **8**A-B will have minimal surface area contact with the walls of Schlemm's canal, i.e., only point contacts at the end of wires or fibers **170**. Alternatively, a support having an open network structure can be at least partially made from a mesh or foam. The mesh or foam can be made of any suitable material, e.g., metal or plastic. As shown in FIGS. **8**C-D, the support can have a sinusoidal or zig-zag configuration extending along a selected length of Schlemm's canal. For the example shown in FIG. **8**C, the support will contact the wall of Schlemm's canal at least three points, labeled P_1, P_2, and P_3, after implantation. In FIGS. **8**E-H, examples of rod-like supports having fluted edges are shown. In FIGS. **8**E-F, fluted edges **110** extend longitudinally along sides **112** between ends **114** of the support to form structures **116**. Structures **116** can include fenestrations **113**. The support can include central bore **117**. In FIGS. **8**G-H, fluted edges **110'** extend along sides **112'** to form structures **116'**. Structures **116'** have serrated outer surfaces **115'** extending between ends **114'**. The support can include central bore **117'**. In the variations illustrated in FIGS. **8**E-H, the support may contact the canal walls at least four points. In some variations, the support is adjustable.

A common characteristic of the support configurations described here is that they need not have continuous or extensive contact with a wall of Schlemm's canal. Indeed, many of the described devices and structures have minimal tangential, periodic, or sporadic contact with the wall. The surface of the support can be rough, smooth, spiked or fluted. As the example shown in FIGS. **8**A-B shows, some supports only

have point contacts with the canal wall. For the supports shown in FIGS. **5**B-C, the rounded beads of each of the supports make only tangential contact with the canal wall. Bead shapes can be selected or designed to have minimal surface area contact with canal walls, e.g., beads **98** having fluted edges as shown in FIGS. **6**A-B may have low surface area contact with canal walls. In addition, supports having widely spaced apart beads, e.g., by connectors illustrated in FIGS. **7**D-E that can function to space beads at desired intervals to reduce contact with canal walls yet operate to keep the canal open. As illustrated above with respect to FIGS. **8**C-D, in some variations, the support contacts the interior wall of the canal at least two points; or at least three points.

Expanded cross-sectional views of a support **152** implanted circumferentially in Schlemm's canal are provided FIGS. **9**A-B. The fraction of canal wall surface area in contact with a support can be estimated by viewing the inside of Schlemm's canal as a slightly arcuate cylinder C having length L, extending circumferentially from a first end X_1 to a second end X_2 of support **152**, and inside radius R_i. In some variations, the support contacts less than 0.1% or less than 1% of the surface area of the cylinder C as described above. In other variations, the support contacts less than 10% of the surface area of C. In still other variations, the support contacts less than 30% of the surface area of C. For example, the support **152** shown in FIGS. **9**A-B contacts the canal wall **62** only at bead outer peripheral edges at E_1-E_7, along a distance of the bead width B_W. There is no contact with the canal walls where connectors **156** space apart beads **154**, and no contact in fluted regions **160** of beads **154**. The design feature of minimal support contact with canal walls allows a support to maintain patency of the canal without substantially interfering with transmural flow across the canal. If a substantial portion of the surface area of the inner periphery of the canal adjacent to the trabecular network or of the surface area of the outer periphery of the canal where the collector channels are located is blocked, effective fluid flow across the canal may be impaired.

Supports can have variable lengths and thicknesses. For example, the length of supports using beads can be tuned by varying the number, type, or spacing of beads, or any combination thereof. The thickness of a support can be increased by adding one or more beads having larger dimensions. Unitary supports can also be built with varying lengths, or with adjustable (e.g., trimmable) dimensions. For example, for a support made of shapeable metal having a sinusoidal or zig-zag configuration as shown FIGS. **8**C-D, a cross-sectional dimension **117** of the support can be decreased or increased by apply tension along dimension **119**. As illustrated in FIG. **10**A, a support **160** can extend essentially around the entire circumference of Schlemm's canal **30**. Alternatively, a support can extend approximately half way around the circumference of the canal (not shown). As shown in FIG. **10**B, a support **162** can extend less than half way around the canal. As shown in FIG. **10**C, a support **164** can extend a quarter or less of the circumference around the canal. In addition, more than one support **164**, **166**, **168** can be inserted into a single Schlemm's canal. If multiple supports are inserted into a single canal, they can be of different shapes, lengths, materials or sizes.

A support can be configured such that it will open the canal beyond a maximum cross-sectional dimension of the support itself. For example, as illustrated in FIG. **11**A, device **130** comprising support **132** is inserted into Schlemm's canal **30**. Support **132** comprises beads **134** which have a maximum cross-sectional dimension B_D. Support **132** comprises a stiff arcuate element **135** with a radius of curvature R_{supp} smaller than the radius of curvature of Schlemm's canal R_{SC}. The smaller, fixed radius of curvature R_{supp} of arcuate member **135** urges canal **30** to open more than B_D. In another variation shown in FIG. **11**B, support **179** comprises an arcuate member **180** without beads having a radius of curvature R_{supp} that is less than the radius of curvature R_{SC} of the canal. Member **180** is sufficiently stiff to urge the canal open. In another variation shown in FIG. **11**C, support **181** comprises an arcuate member **182** having a radius of curvature R_{supp} larger than that of Schlemm's canal R_{SC}. Member **182** is also sufficiently stiff to urge the canal open. Arcuate members **135**, **180** and **182** can comprise a shape memory material such as Nitinol, for example. As indicated in FIG. **11**C, support **181** can include beads **184**. To urge open the canal, the radius of curvature R_{supp} of an arcuate members can be about 10%, 20%, 30%, 40%, or 50% or smaller or larger than that of Schlemm's canal R_{SC}. For example, an arcuate member can have a radius of curvature of about 3 mm to about 8 mm. In some variations, the radius of curvature of an arcuate member R_{supp} in a support is about 3 mm, or about 4 mm, or about 5 mm. In other variations, the radius of curvature R_{supp} of an arcuate member in a support is about 6 mm, or about 7 mm, or about 8 mm.

The supports described here occupy at least a portion of a central core of Schlemm's canal. The central core of Schlemm's canal is the region around the cross-sectional center of the canal in the interior space of the canal lumen. A support that occupies at least a portion of the central core of the canal can traverse at least a portion of the canal lumen. For example, some variations of supports can traverse the cross-sectional center of the canal at least one point. Referring to FIG. **12**A, a front view of a support **220** having beads **222** connected with connectors **224** is provided. FIG. **12**B shows an expanded cross-sectional view along line II-II'. Support **220** occupies a portion canal central core **67** in canal lumen **64**. Trabecular meshwork **28** is shown adjacent to canal **30**. In this variation, support **220** traverses the cross-sectional center **66** of the canal. In other variations, supports can traverse the lumen of the canal off-center, e.g., appearing as a chord across the canal lumen in cross-section. Referring to FIG. **12**C, a front view of an arcuate support **210** is shown. FIG. **12**D shows an expanded cross-sectional view along line III-III'. Support **210** traverses and occupies a portion of central core **67** in lumen **64** of canal **30** without passing through canal center **66**. In some variations, the support can occupy the majority of the central core of the canal. Referring to FIG. **12**E, a front view of support **230** comprising disc-like beads **232** is shown. A cross-sectional view along line IV-IV' is shown in FIG. **12**F. As illustrated in FIG. **12**F, bead **232** with fenestrations **234** occupies the majority of central core **67** of canal **30**. In other variations, the support occupies only a small portion of the central core of the canal. For example, in FIG. **12**G, a front view of a support **240** having an open network structure is shown. A cross-sectional view along line V-V' is shown in FIG. **12**H.

A support can made of a variety of different materials. In general, the support should comprise a biocompatible material, such as a biocompatible polymer, ceramic or ceramic composite, glass or glass composite, metal, or combinations of these materials. Examples of biocompatible metals include stainless steel, gold, silver, titanium, tantalum, platinum and alloys thereof, cobalt and chromium alloys, and titanium nickel alloys such as Nitinol. Examples of biocompatible polymers include high density polyethylene, polyurethane, polycarbonate, polypropylene, polymethylmethacrylate, polybutylmethacrylate, polyesters, polytetrafluoroethylene, silicone, polyvinyl alcohol, polyvinyl pyrrolidone, polyvinyl chloride, ethyl vinyl acetate, collagen, collagen derivatives,

flexible fused silica, polyolefins, NYLON® polymer, polyimide, polyacrylamide, fluorinated elastomers, and copolymers and blends thereof. In addition, biocompatible hydrogels can be used in supports and devices described herein. As discussed in more detail below, biocompatible polymers may be biodegradable. A support can be made of a single material or a combination of materials. In some variations, a support made from a first material is coated with a second material, e.g., to enhance or improve its biocompatibility.

In some examples, the biocompatible polymer in a support will include a biodegradable polymer. Examples of suitable biodegradable polymers include collagen, a collagen derivative, a poly(lactide), a poly(glycolide), a poly(lactide-co-glycolide), a poly(lactic acid), a poly(glycolic acid), a poly(lactic acid-co-glycolic acid), a poly(lactide)/poly(ethylene glycol) copolymer, a poly(glycolide)/poly(ethylene glycol) copolymer, a poly(lactide-co-glycolide)/polyethylene glycol) copolymer, a poly(lactic acid)/poly(ethylene glycol) copolymer, a poly(glycolic acid)/poly(ethylene glycol) copolymer, a poly(lactic acid-co-glycolic acid)/poly(ethylene glycol) copolymer, a poly(caprolactone), a poly(caprolactone) poly (ethylene glycol) copolymer, a polyorthoester, a poly(phosphazene), a poly(hydroxybutyrate) or a copolymer including a poly(hydroxybutyrate), a poly(lactide-co-caprolactone), a polycarbonate, a poly(esteramide), a polyanhydride, a poly (dioxanone), a poly(alkylene alkylate), a copolymer of polyethylene glycol and a polyorthoester, a biodegradable polyurethane, a poly(amino acid), a polyetherester, a polyacetal, a polycyanoacrylate, a poly(oxyethylene)/poly(oxypropylene) copolymer, and blends and copolymers thereof.

At least a portion of the support can be made from a shape memory material. For example, shape memory alloys, e.g. a nickel-titanium alloy can be used. In addition, shape memory polymers, e.g., polymers made from copolymerizing monomers oligo(e-caprolactone) dimethacrylate and n-butyl acrylate or polymers based on styrene acrylate, cyanate ester and epoxies, can be used. If a shape memory material is used in the support, the support can have a compressed state prior to and during implantation, and an expanded state following implantation. The use of a compressed state support comprising a shape memory material can allow for a smaller incision and facilitate insertion into a narrowed or compressed Schlemm's canal. Once implanted, the support can be expanding using any suitable method, e.g., thermally activated by body heat or an alternate heat source, to adopt an expanded state, thereby opening the canal.

The support can include an active agent, such as a pharmaceutical. Active agents can include prostaglandins, prostaglandin analogs, beta blockers, alpha-2 agonists, calcium channel blockers, carbonic anhydrase inhibitors, growth factors, such as tissue growth factors and vascular endothelial growth factors, anti-metabolites, chemotherapeutic agents such as mitomycin-C,5-fluorouracil, steroids, antagonists of growth factors such as antagonists of vascular endothelial growth factors, or combinations thereof. The active agent can be provided as a coating on at least a portion of a support. The active agent can be delivered throughout the eye by dissolution or other dispersal mechanisms. Alternatively, at least a portion of the support can be impregnated with the active agent. In other embodiments, the active agent can be dispersed within at least a portion of the support. For example, a cavity in the support can be filled with the active agent.

The delivery of the active agent can be controlled by time-release. For example, the portion of the support containing the active agent can include a time release coating or time release formulation designed to gradually dissipate the active agent over a certain period of time. Biodegradable coatings and formulations for time-release of active agents are known in the art. In some variations, the support can comprise multiple layers, where the layers each comprise an active agent. For example, support layers can be used to release a series of different agents, or a series of doses of the same agent. Such layers can be part of a coating applied to a support, or part of a support body. In addition, the support can comprise biodegradable layers containing no active agent that can be applied or interspersed between other layers to further control delivery of active agents to the eye.

In some variations, it will be desirable to change or alter the support using electromagnetic radiation. For example, at least a portion of a support can be fenestrated, perforated, bent, shaped or formed using a laser to enhance intraocular pressure reduction. As illustrated in FIG. **13**, predetermined localized portions **120** of support **122** can be designed to absorb light of a certain wavelength or wavelength range. Preferential absorption can be achieved by material selection and/or by doping with chromophores. Upon irradiation with sufficient energy at the selected wavelength or wavelength range, the patterned regions **120** will ablate or melt, leaving new or enlarged perforations or indentations in the support. For example, a pulsed titanium sapphire laser operating between about 750 and about 800 nm can be used to ablate gold regions. If beads **126** in support **120** are hollow, then after irradiation and ablation, features **120** will become fenestrations. The fenestrations can be created to make support **122** more porous in nature or to allow release of an active agent from within a support, e.g., from within beads **126**. Alternatively, it is possible to use a mask in combination with electromagnetic radiation to alter a support, such as by patterning or machining. The modification of a support using electromagnetic radiation can be carried out prior to or subsequent to insertion.

In some variations, the visual appearance of the support can be enhanced under certain conditions to facilitate placement or to monitor the position or condition of the support. Visual enhancement can be achieved by incorporating into or onto the support chromophores that fluoresce or phosphoresce upon excitation with a light source. Chromophores can also assist a clinician in verifying the position of the support postoperatively using a gonioscope, for example. Light sources can include lasers, lamps, and light emitting diodes. In some instances, transmission or absorption filters may be used to select the wavelength of the excitation source or to detect or view emission. Emission from a support capable of visual enhancement may be in the wavelength range of about 300 nm to about 800 nm. The chromophores can be an integral component of the material making up the support, doped into support material, or coated or sprayed onto the support. Visually-enhancing chromophores can be applied on a temporary basis, or on a permanent basis. An example of a suitable chromophore is fluorescein, which can be excited with any laser or lamp emitting at about 400 to about 500 nm. In addition, phosphorus-based chemiluminescent or photoluminescent pigments can be used, which can be selected to absorb at various wavelengths across the visible spectrum.

In some variations, the support may be capable of being attached to tissue. For example, the support may include a hook, loop, clip, extension, or the like that may be easily attached to tissue. The support may also be attached to tissue using sutures or adhesives. The support may be attached to tissue using more than one attachment method, e.g., suturing may be used in combination with a loop, or an adhesive may be used in combination with a hook. In other variations, the

support may be allowed to self-position in Schlemm's canal. In still other variations, the support may be mobile within Schlemm's canal.

Kits

Kits for reducing intraocular pressure are provided, where the kits contain at least one support that can be implanted circumferentially within Schlemm's canal configured to maintain the patency of at least a portion of Schlemm's canal. The support occupies at least a portion of a central core of Schlemm's canal and does not substantially interfere with transmural flow across the canal. The kits also provide an introducer or delivery device for implanting the support in the canal. The support and introducer are provided in packaged combination in the kits. The kits can also include instructions for use, e.g., for implanting and inspecting the support.

The introducer can be inserted into the eye and is capable of implanting the support at the desired implantation position within Schlemm's canal. For example, an introducer may include a tubular cannula through which the support may be passed. In addition to a cannula, the introducer may include a tubular or solid pusher rod that can be used to push or advance the support into and/or around Schlemm's canal. Alternatively, a pusher rod or plunger can be used without a cannula to introduce a support into the canal. A support can be installed into the lumen of a cannula prior to insertion, the distal end of the cannula positioned at or near the desired support location, and the pusher rod operated from the proximal end to push the support distally out of the distal end of the cannula and into the canal. The cannula and/or the pusher rod may be flexible and small enough in diameter to extend at least partially around the canal. In some variations, a proximal end of a suture can be introduced into the canal via a cannula and the suture extended circumferentially around the canal. A distal portion of the suture can be connected to the support and force applied to the proximal end of the suture to pull the support into the canal. The support can then be positioned within the canal by pulling the suture in a distal or proximal direction. The suture can be used to anchor the support within the canal. In other variations, the support can be directly introduced into the canal using surgical forceps, or the like.

FIGS. **14**A-D illustrate additional variations for introducing a support into the canal. As shown in FIG. **14**A, a support **200** can be introduced into the canal using syringe **202** and plunger **204**. Syringe **202** has distal end **206** that can be at least partially inserted into or placed adjacent to an opening in the canal. Force in a distal direction is applied to plunger **204**, thereby pushing support **200** into the canal. Referring to FIGS. **14**B-C, distal end **208** of guide element **210** can be at least partially introduced into the canal. Guide element **210** can be a guide wire. Guide element **210** can be extended circumferentially along the canal to aid in positioning the support. Support **212** comprises central bore **218** capable of accommodating guide element **210** such that support **212** can be threaded onto guide element **210** and slidably positioned along the guide element. Once distal end **209** of support **212** is threaded onto guide element **210**, support **212** can be pushed in a distal direction along guide element **210** to insert support **212** into the canal. In some variations, support **212** can remain threaded onto guide element **210**, and guide element **210** can remain in the canal. In other variations, support **212** can be slid off distal end **208** of guide element **210**, and the guide element can be pulled in a proximal direction for removal. Referring to FIGS. **14**C-D, syringe **202** with plunger **204** can be used in combination with a guide element **210**. In this variation, distal end **208** of guide element **210** is inserted at least partially into Schlemm's canal. Guide element **210** can be extended circumferentially along the canal to aid in positioning the support. Support **212** has central bore **218** capable of accommodating guide element **210**. Proximal end **211** of guide element **210** is inserted into bore **218**. Plunger **204** is depressed in a distal direction to push support **212** into the canal and slide support **212** along element **210**. Guide element **210** can remain in the canal or be removed following insertion of the support. Supports **200**, **212** must be sufficiently resilient to withstand force encountered as they are pushed into the canal.

In some variations, a positioning device may be used with the introducer to position or adjust the support within the canal. A positioning device can include a rod, grippers, a clamp, a hook, or the like. In other variations, a device or system capable of dilating the canal to facilitate insertion of a support may be included in the kits, e.g., a syringe or other device capable of injecting fluid into the canal.

In some variations, the kits contain at least two supports. Multiple supports can be implanted within one eye or within multiple eyes. If the kits contain multiple supports, the kits may also contain multiple introducers. Alternatively, the same introducer may be used for implantation of multiple supports, especially if the multiple supports are being delivered to a single eye. If multiple supports are to be delivered with the same introducer, then the multiple supports can be preloaded into the introducer for sterility. If more than one support is included in a kit, the supports may be of different shapes, sizes, lengths, or materials. If the kits contain more than one support to be implanted into a single eye, the supports can be connected together.

The kits can comprise an active agent, such as a pharmaceutical agent. The active agent may be included as an integral part of the support, or may be supplied in kits for application to the support or to the eye during or after implantation. Examples of active agents that may be supplied as part of the kits include prostaglandins, prostaglandin analogs, beta blockers, alpha-2 agonists, calcium channel blockers, carbonic anhydrase inhibitors, growth factors, such as tissue growth factors or vascular endothelial growth factors, antimetabolites, chemotherapeutic agents such as mitomycin-C, 5-fluorouracil, steroids, antagonists of growth factors, such as antagonists of vascular endothelial growth factor, and combinations thereof.

The kits may contain a fixation device for attaching a support to tissue. Such a fixation device can include sutures, hooks, barbs, clips, adhesives, and combinations thereof. In addition, the kits may include a system for visually enhancing the support to facilitate viewing, positioning, and monitoring of a support. A system for visually enhancing the support can include a light source, a transmission or absorption filter, a mirror, a composition comprising a chromophore capable of fluorescing or phosphorescing that can be applied to the support, or any combination thereof. Chromophores can assist a clinician in verifying the position of the support postoperatively using a gonioscope, for example. The light source is capable of exciting a chromophore contained within or on the support such that the chromophore emits fluorescence or phosphorescence. The emission is preferably within the wavelength range of about 300 nm to about 800 nm. A suitable light source for such a system can comprise a laser, a light emitting diode, or a lamp. In some instances, transmission or absorption filters may be used to further select the wavelength range of the excitation source or view or detect emission from chromophores. One or more minors may be used to direct a light source or emitted light, or to view the support.

Methods

Methods for reducing intraocular pressure are also provided. In general, the methods comprise inserting a support circumferentially within Schlemm's canal, such that the support maintains the patency of at least a portion of the canal. The support occupies at least a portion of a central core of Schlemm's canal and does not substantially interfere with transmural flow across Schlemm's canal.

The methods can comprise inserting a support circumferentially into Schlemm's canal using an introducer and/or a positioning device. The introducer can include a cannula and a tubular or hollow pusher rod. The support can be installed in the lumen of the cannula at its distal end and the pusher rod can be inserted into the lumen of the cannula at its proximal end and extended distally to push the support into position in the canal. In some instances, the cannula and/or the pusher rod may be flexible and small enough in diameter to at least partially extend circumferentially around the canal. In some variations of the methods, a positioning device can be used in addition to an introducer. The positioning device can comprise a second rod, a gripper, a hook, a clamp, or the like. In some variations, the methods include illuminating a support with a light source to causes the support to fluoresce or phosphoresce, thus aiding the visual appearance of the support. The illuminating of the support can occur during or after implantation to inspect the support, e.g., to monitor its position, condition, or performance.

In some instances, the methods will also comprise dilating Schlemm's canal prior to insertion of the support. Dilation of the canal can be accomplished by injecting fluid into the canal. For example, a high viscosity fluid such as sodium hyaluronate, or other dilating fluids known in the art, can be used to dilate the canal.

The methods may include implanting more than one support into an eye. In some variations, the methods will include implantation of two or more supports circumferentially adjacent to each other within the canal, and in other variations, the methods will include implantation of supports circumferentially opposed to each other within the canal, e.g., two supports centered about 180° apart around the circumference of Schlemm's canal. Some variations of the methods can comprise connecting together multiple supports in a single eye.

In some variations, the methods can include anchoring the support to tissue surrounding Schlemm's canal. Anchoring the support to tissue can be accomplished in a variety of ways, e.g., by suturing, application of adhesives, installation of hooks, clips, or the like, or combinations thereof. In other variations, the methods can comprise selecting the size of the support such that the support fits securely into the canal by a friction fit. Examples of arcuate supports that can be implanted with a friction fit are illustrated in FIGS. **11**A-C.

The methods described here can also include altering the support using electromagnetic radiation. For example, a support can include regions capable of preferentially absorbing a certain wavelength range. When electromagnetic radiation of the appropriate wavelength range with sufficient energy is incident upon the support, material in the preferentially absorbing regions will melt or ablate, resulting in perforations or indentations in the support at those regions. For example, a pulsed titanium sapphire laser emitting at about 750 nm to about 800 nm incident on gold can cause the gold to melt or ablate. The alteration of the support using electromagnetic radiation can occur before or after implantation of a support. For example, fenestrations can be created or enlarged in a support after the support has remained in an eye for a period of time to enhance drainage.

While the inventive devices, kits and methods have been described in some detail by way of illustration, such illustration is for purposes of clarity of understanding only. It will be readily apparent to those of ordinary skill in the art in light of the teachings herein that certain changes and modifications may be made thereto without departing from the spirit and scope of the appended claims. For example, it is envisioned that the devices, kits and methods can be applied to nonhuman eyes to reduce intraocular pressure, e.g., in dogs, cats, primates, or horses.

What we claim is:

1. A device comprising:

a support having at least one fenestration that is longitudinally insertable into a lumen of Schlemm's canal, the support having a cross-sectional dimension sufficient to at least partially prop open Schlemm's canal upon insertion into the canal, and to thereby maintain patency of at least a portion of the canal so that fluid may traverse the canal without substantial interference from the support, wherein when the support is disposed within a lumen of Schlemm's canal, contact between the support and a wall of the canal is discontinuous along a perimeter of the lumen of the canal, and wherein when the support is disposed within a cylindrical section of the lumen of the canal having an internal wall surface area C, the support contacts less than 30% of C.

2. The device of claim **1**, wherein the support makes minimal contact with the interior surface of the canal wall when the support is disposed within the lumen of the canal.

3. The device of claim **1**, wherein the support makes only tangential contact with the canal wall when the support is disposed within the lumen of the canal.

4. The device of claim **1**, wherein the support makes only point contacts with the wall of the canal when the support is disposed within the lumen of the canal.

5. The device of claim **1**, wherein the support comprises fluted edges.

6. The device of claim **5**, wherein only outer peripheral edges of the support contact the canal wall when the support is disposed within the lumen of the canal.

7. The device of claim **1**, wherein the support comprises elements that make periodic contact with the canal wall when the support is disposed within the lumen of the canal.

8. The device of claim **1**, wherein the support comprises a biocompatible metal.

9. The device of claim **1**, wherein the support comprises a biocompatible polymer.

10. The device of claim **1**, wherein the support comprises a shape memory material.

11. The device of claim **10**, wherein the support comprises a nickel titanium alloy.

12. The device of claim **10**, wherein the support is compressible into a first configuration and expandable into a second configuration.

13. The device of claim **12**, wherein the support is adapted to be thermally activated to be expanded into the second configuration.

14. The device of claim **1**, wherein the support comprises a metal wire.

15. The device of claim **1**, wherein the support has a unitary structure.

16. The device of claim **15**, wherein the support has a sinusoidal or zig-zag configuration.

17. The device of claim **1**, wherein the support has an open network structure.

18. The device of claim **1**, wherein the support comprises multiple connected elements configured to be distributed lon-

gitudinally along Schlemm's canal when the device is in use, and wherein at least one of the connected elements has a cross-sectional dimension sufficient to at least partially prop open Schlemm's canal, and to thereby maintain patency of at least a portion of the canal.

19. The device of claim **18**, wherein when the support is disposed within the lumen of Schlemm's canal, at least one region of the support that is located between first and second adjacent connected elements does not contact the wall of the canal.

20. The device of claim **18**, wherein at least one of the connected elements is ovoid.

21. The device of claim **18**, wherein the at least one fenestration is included in at least one of the connected elements.

22. The device of claim **1**, wherein the support is configured to be disposed entirely within Schlemm's canal.

23. The device of claim **1**, wherein at least a portion of the support is porous.

24. The device of claim **1**, wherein the support contacts less than 10% of C.

25. The device of claim **1**, wherein the support contacts less than 1% of C.

26. The device of **1**, wherein the support comprises an active agent.

27. The device of claim **26**, wherein the active agent comprises a prostaglandin.

28. The device of claim **26**, wherein the active agent comprises a prostaglandin analog.

29. The device of claim **1**, wherein the support occupies at least a portion of a central core of the canal.

30. The device of claim **1**, wherein at least a portion of the support has a polyhedral shape.

31. The device of claim **1**, wherein the support is non-tubular.

32. A device comprising:

a support having at least one fenestration that is longitudinally insertable into a lumen of Schlemm's canal, the support comprising an exterior surface and having a cross-sectional dimension sufficient to at least partially prop open Schlemm's canal upon insertion into the canal, and to thereby maintain patency of at least a portion of the canal so that fluid may traverse the canal without substantial interference from the support,

wherein when the support is disposed within a lumen of Schlemm's canal, only a portion of the exterior surface of the support contacts an inner periphery of the lumen of the canal, and wherein when the support is disposed within a cylindrical section of the lumen of the canal having an internal wall surface area C, the support contacts less than 30% of C.

33. The device of claim **32**, wherein the support makes minimal contact with the interior surface of the canal wall when the support is disposed within the lumen of the canal.

34. The device of claim **32**, wherein the support makes only tangential contact with a wall of the canal when the support is disposed within the lumen of the canal.

35. The device of claim **32**, wherein the support makes only point contacts with a wall of the canal when the support is disposed within the lumen of the canal.

36. The device of claim **32**, wherein the support comprises fluted edges.

37. The device of claim **36**, wherein only outer peripheral edges of the support contact the wall of the canal when the support is disposed within the lumen of the canal.

38. The device of claim **32**, wherein the support comprises elements that make periodic contact with the canal wall when the support is disposed within the lumen of the canal.

39. The device of claim **32**, wherein the support comprises a biocompatible metal.

40. The device of claim **32**, wherein the support comprises a biocompatible polymer.

41. The device of claim **32**, wherein the support comprises a shape memory material.

42. The device of claim **41**, wherein the support comprises a nickel titanium alloy.

43. The device of claim **41**, wherein the support is compressible into a first configuration and expandable into a second configuration.

44. The device of claim **43**, wherein the support is adapted to be thermally activated to be expanded into the second configuration.

45. The device of claim **32**, wherein the support comprises a metal wire.

46. The device of claim **32**, wherein the support has a unitary structure.

47. The device of claim **46**, wherein the support has a sinusoidal or zig-zag configuration.

48. The device of claim **32**, wherein the support has an open network structure.

49. The device of claim **32**, wherein the support comprises multiple connected elements configured to be distributed longitudinally along Schlemm's canal when the device is in use, and wherein at least one of the connected elements has a cross-sectional dimension sufficient to at least partially prop open Schlemm's canal, and to thereby maintain patency of at least a portion of the canal.

50. The device of claim **49**, wherein when the support is disposed within the lumen of Schlemm's canal, at least one region of the support that is located between first and second adjacent connected elements does not contact the wall of the canal.

51. The device of claim **49**, wherein at least one of the connected elements is ovoid.

52. The device of claim **49**, wherein the at least one fenestration is included in at least one of the connected elements.

53. The device of claim **32**, wherein the support is configured to be disposed entirely within Schlemm's canal.

54. The device of claim **32**, wherein at least a portion of the support is porous.

55. The device of claim **32**, wherein the support contacts less than 10% of C.

56. The device of claim **32**, wherein the support contacts less than 1% of C.

57. The device of **32**, wherein the support comprises an active agent.

58. The device of claim **57**, wherein the active agent comprises a prostaglandin.

59. The device of claim **57**, wherein the active agent comprises a prostaglandin analog.

60. The device of claim **32**, wherein the support occupies at least a portion of a central core of the canal.

61. The device of claim **32**, wherein at least a portion of the support has a polyhedral shape.

62. The device of claim **32**, wherein the support is non-tubular.

63. A method for reducing intraocular pressure in an eye, the method comprising:

inserting a support having at least one fenestration into a lumen of Schlemm's canal to at least partially prop open the canal and thereby maintain patency of at least a portion of the canal,

wherein when the support is disposed within the lumen of Schlemm's canal, the support allows fluid to traverse the canal without substantial interference from the support,

and wherein contact between the support and a wall of the canal is discontinuous along a perimeter of the lumen of the canal, and wherein when the support is disposed within a cylindrical section of the lumen of the canal having an internal wall surface area C, the support contacts less than 30% of C.

64. The method of claim **63**, the method comprising inserting the support into the lumen of Schlemm's canal such that the support is disposed entirely within the canal.

65. The method of claim **63**, wherein the support makes minimal surface area contact with the canal wall when the support is disposed within the lumen of the canal.

66. The method of claim **63**, wherein the support makes only tangential contact with the wall of the canal when the support is disposed within the lumen of the canal.

67. The method of claim **63**, wherein the support makes only point contacts with the wall of the canal with the support is disposed within the lumen of the canal.

68. The method of claim **63**, wherein the support comprises fluted edges that contact the wall of the canal.

69. The method of claim **63**, wherein the support comprises elements that make periodic contact with the canal wall when the support is disposed within the lumen of the canal.

70. The method of claim **63**, wherein the support has a unitary structure.

71. The method of claim **70**, wherein the support has a sinusoidal or zig-zag structure.

72. The method of claim **63**, wherein the support comprises a metal wire.

73. The method of claim **63**, wherein the support comprises multiple connected elements distributed longitudinally along Schlemm's canal when the support is disposed within the lumen of the canal, and wherein at least one of the elements has a cross-sectional dimension sufficient to at least partially prop open the canal to thereby maintain patency of at least a portion of the canal.

74. The method of claim **63**, wherein the support contacts less than 10% of C.

75. The method of claim **63**, wherein the support contacts less than 1% of C.

76. The method of claim **63**, wherein the support has an open network structure.

77. The method of claim **63**, wherein the support comprises a biocompatible metal.

78. The method of claim **63**, wherein the support comprises a biocompatible polymer.

79. The method of claim **63**, wherein the support comprises a shape memory material.

80. The method of claim **79**, wherein the shape memory material comprises a nickel titanium alloy.

81. The method of claim **79**, wherein the support is compressible into a first configuration and expandable into a second configuration.

82. The method of claim **79**, wherein the support is adapted to be thermally activated to be expanded into the second configuration.

83. The method of claim **63**, wherein the support delivers an active agent to the eye.

84. The method of claim **83**, wherein the active agent comprises a prostaglandin.

85. The method of claim **83**, wherein the active agent comprises a prostaglandin analog.

86. The method of claim **63**, wherein the support occupies at least a portion of a central core of the canal.

* * * * *

EXHIBIT 2

US009370443B2

(12) **United States Patent**
Badawi et al.

(10) **Patent No.: US 9,370,443 B2**
(45) **Date of Patent: Jun. 21, 2016**

(54) **INTRAOCULAR IMPLANTS AND METHODS AND KITS THEREFOR**

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(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 868 days.

(21) Appl. No.: **13/025,112**

(22) Filed: **Feb. 10, 2011**

(65) **Prior Publication Data**

US 2011/0130831 A1 Jun. 2, 2011

Related U.S. Application Data

(62) Division of application No. 11/475,523, filed on Jun. 26, 2006, now Pat. No. 7,909,789.

(51) **Int. Cl.**
A61M 5/00 (2006.01)
A61F 9/007 (2006.01)

(52) **U.S. Cl.**
CPC ***A61F 9/00781*** (2013.01); *A61F 2210/0004* (2013.01); *A61F 2210/0014* (2013.01); *A61F 2250/0067* (2013.01)

(58) **Field of Classification Search**
CPC A61F 9/00781; A61F 2210/0014; A61F 2250/0067
USPC 604/8, 9, 264; 623/23.64, 23.7
See application file for complete search history.

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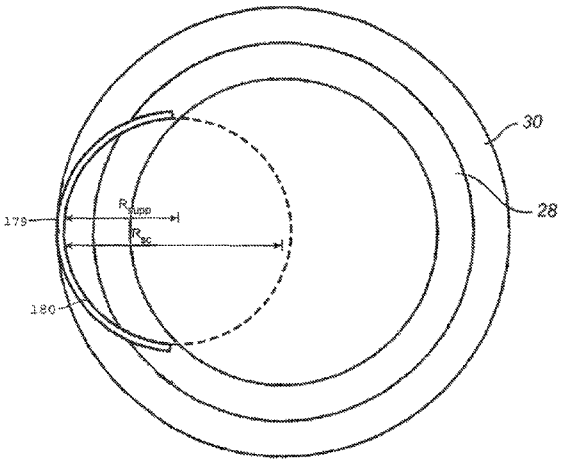
(57) **ABSTRACT**

Devices, methods and kits are described for reducing intraocular pressure. The devices include a support that is implantable within Schlemm's canal and maintains the patency of the canal without substantially interfering with transmural fluid flow across the canal. The devices utilize the natural drainage process of the eye and can be implanted with minimal trauma to the eye. Kits include a support and an introducer for implanting the support within Schlemm's canal. Methods include implanting a support within Schlemm's canal, wherein the support is capable of maintaining the patency of the canal without substantial interference with transmural fluid flow across the canal.

71 Claims, 16 Drawing Sheets



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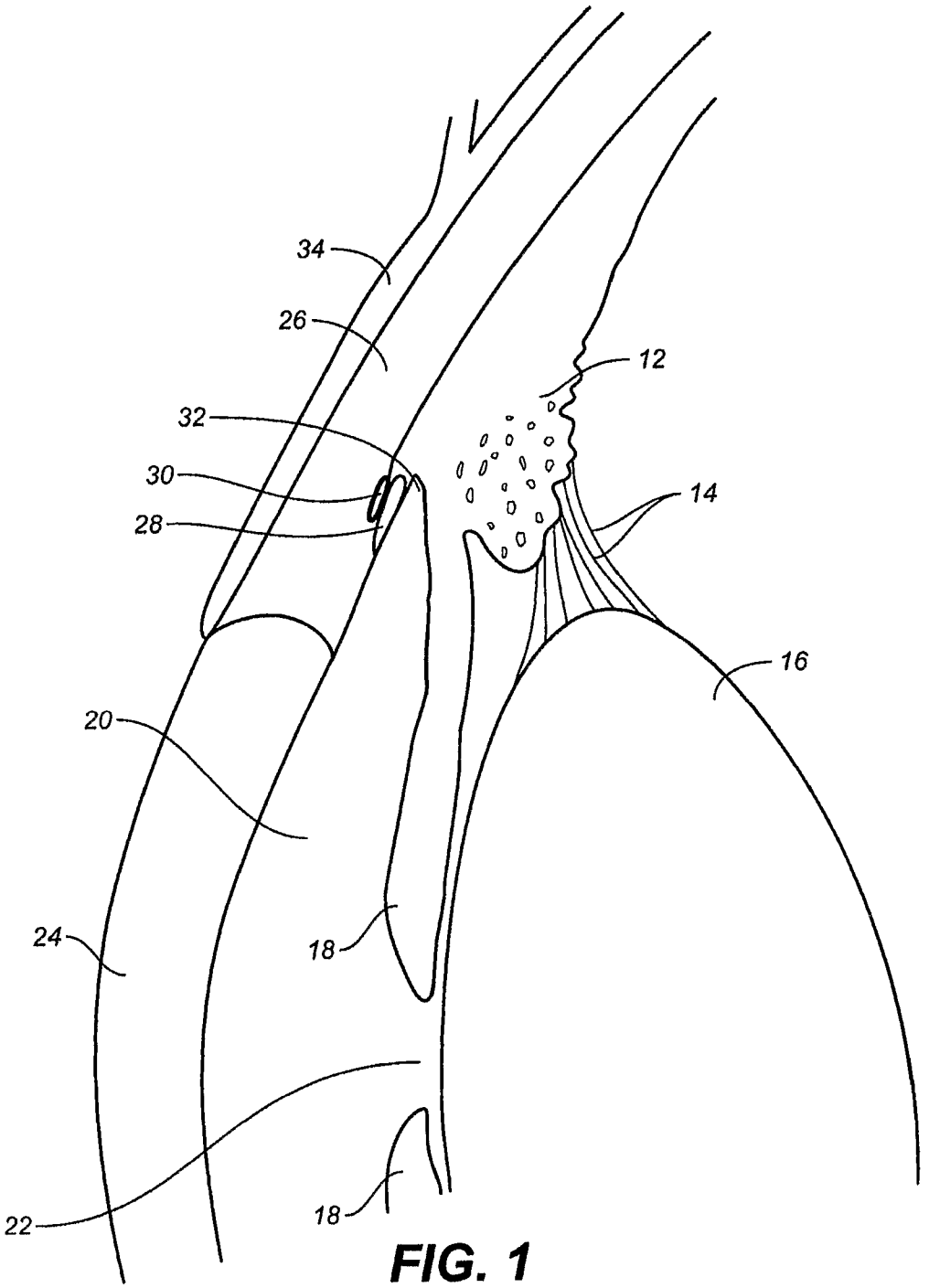

FIG. 1

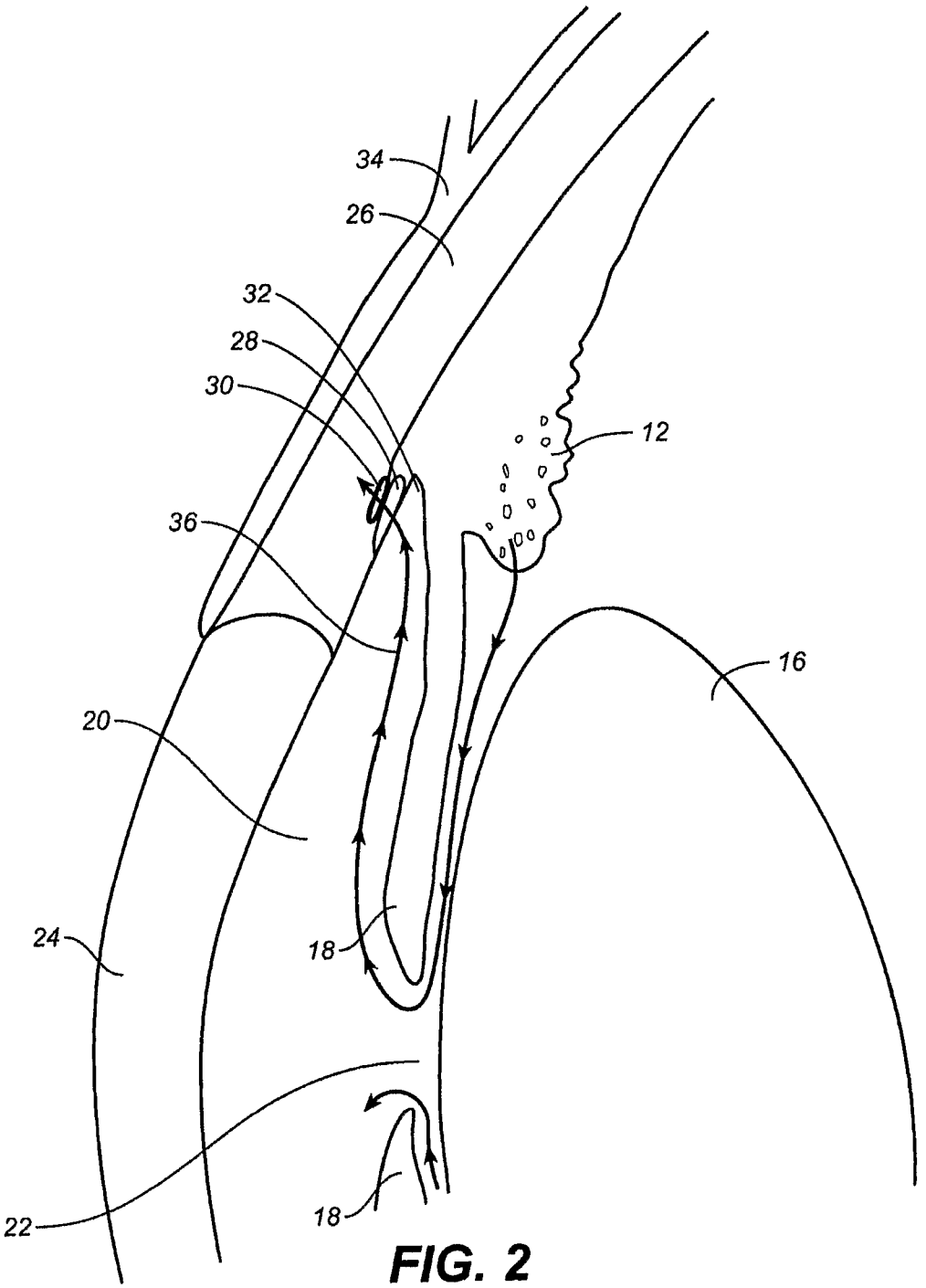

FIG. 2

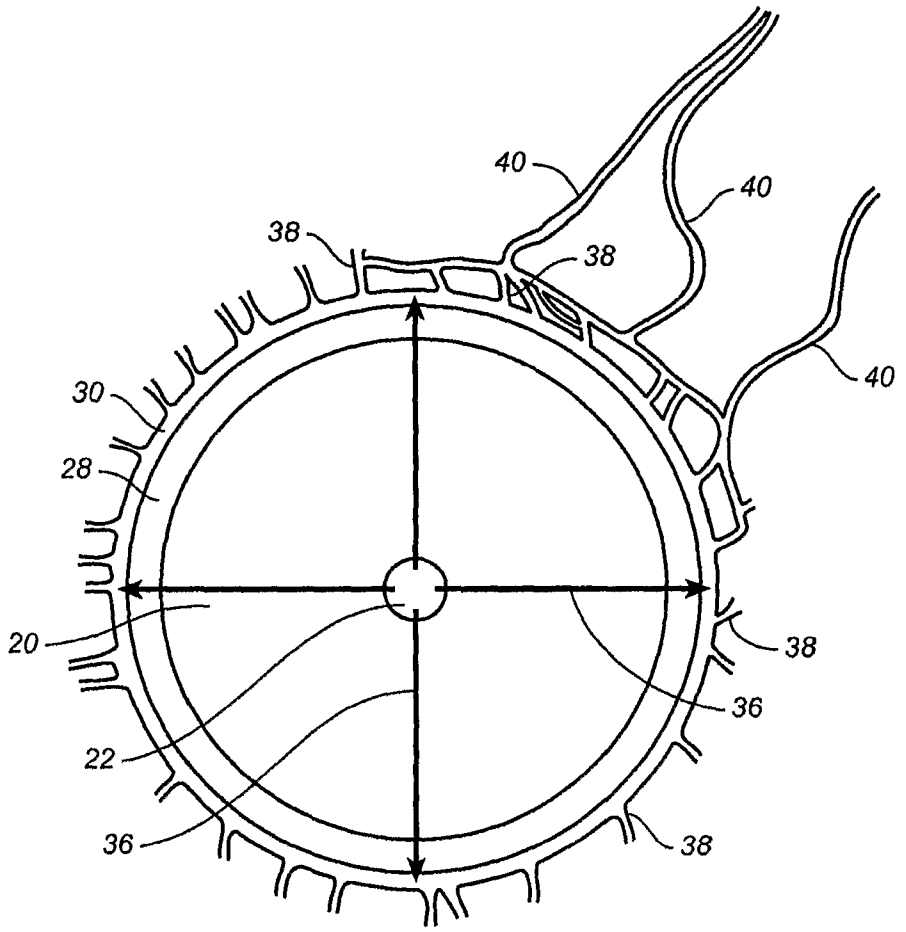

FIG. 3

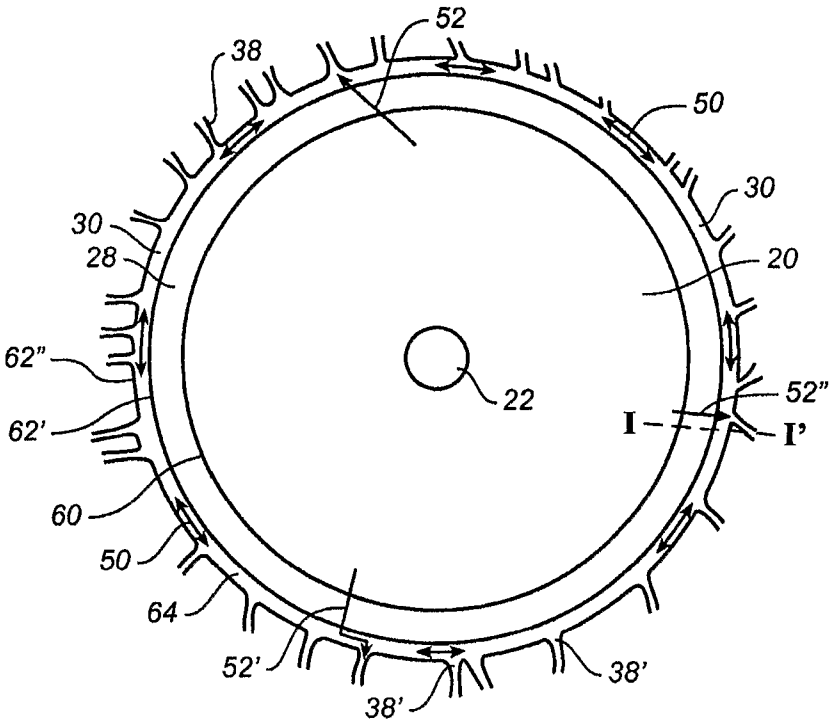
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FIG. 4A

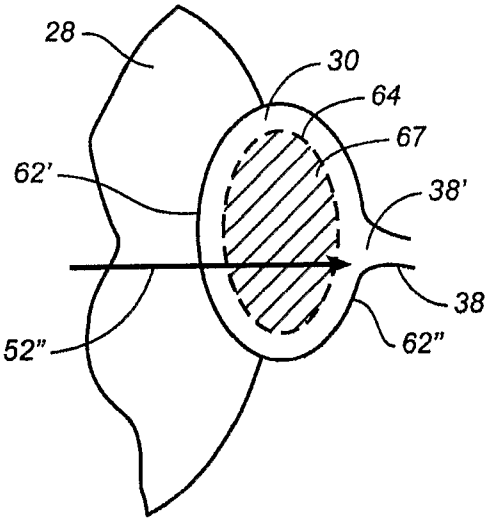
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FIG. 4B

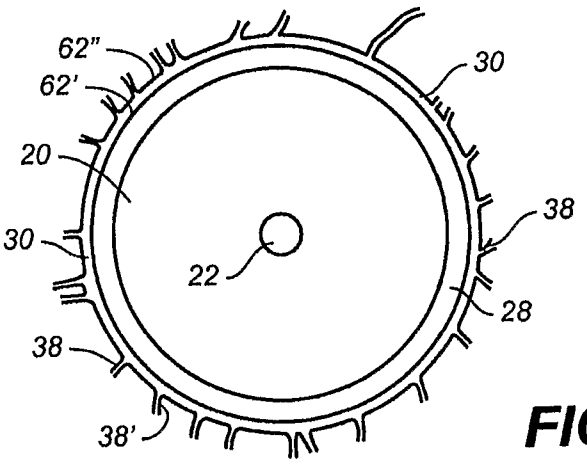


FIG. 5A

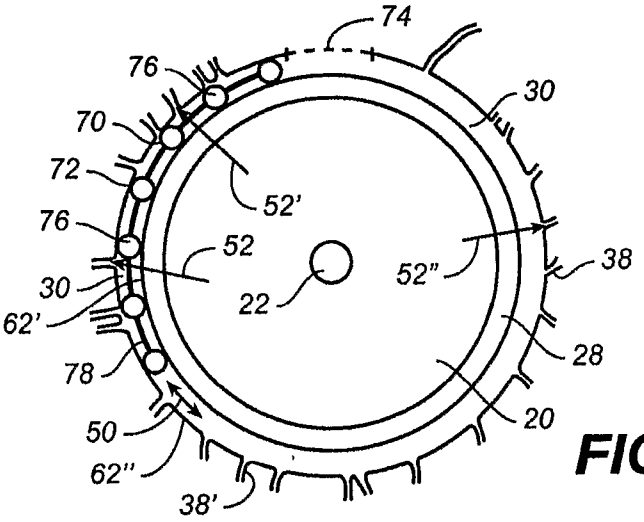


FIG. 5B

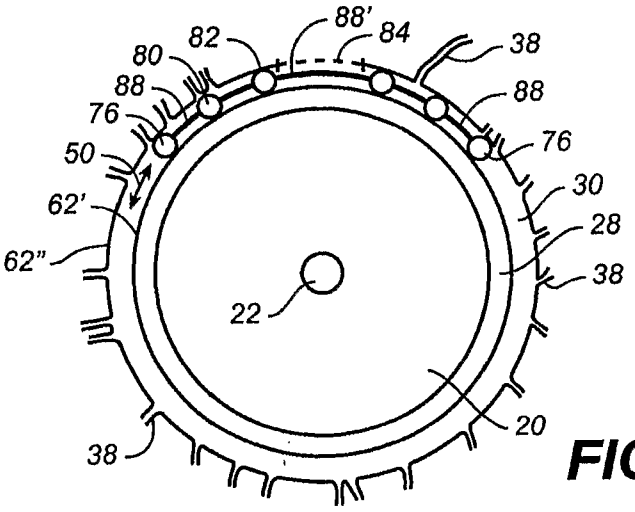


FIG. 5C

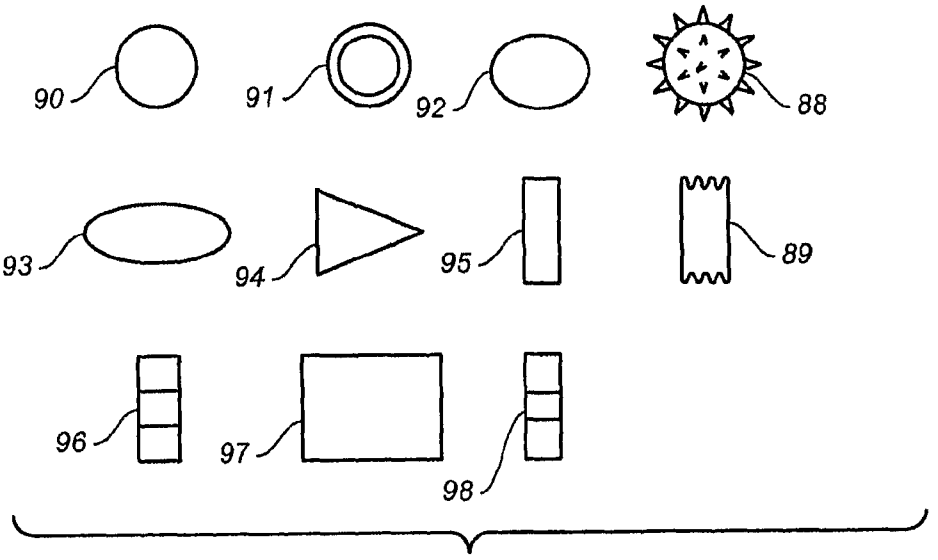


FIG. 6A

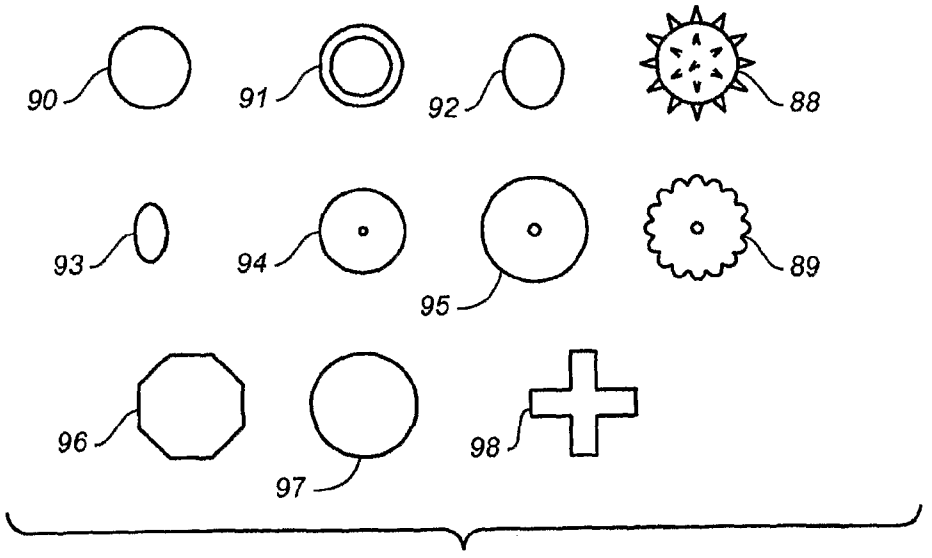


FIG. 6B

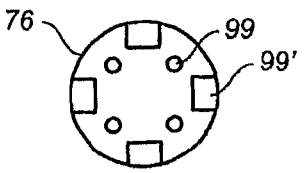


FIG. 6C

FIG. 7A

FIG. 7B

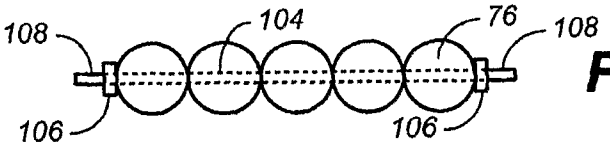


FIG. 7C

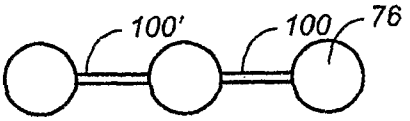


FIG. 7D

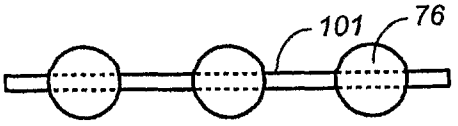


FIG. 7E

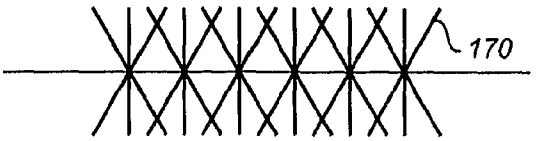


FIG. 8A

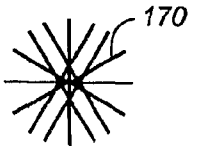


FIG. 8B

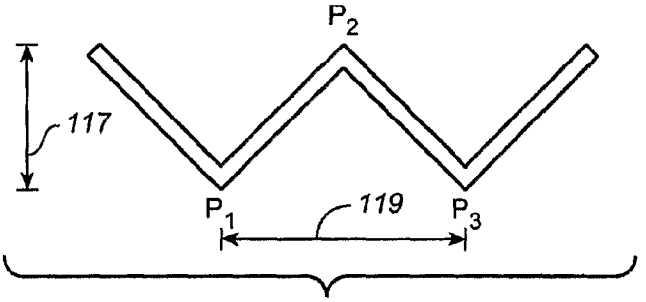


FIG. 8C

FIG. 8D

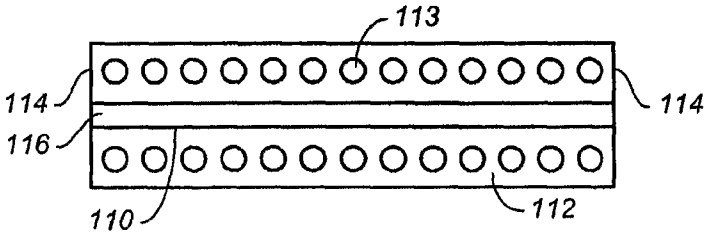


FIG. 8E

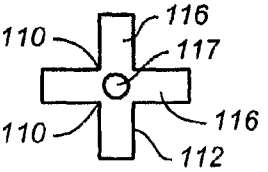


FIG. 8F

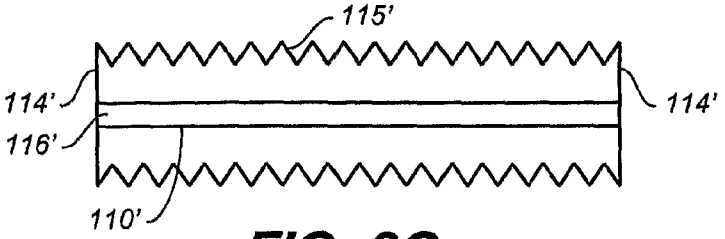


FIG. 8G

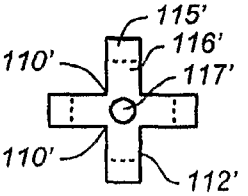
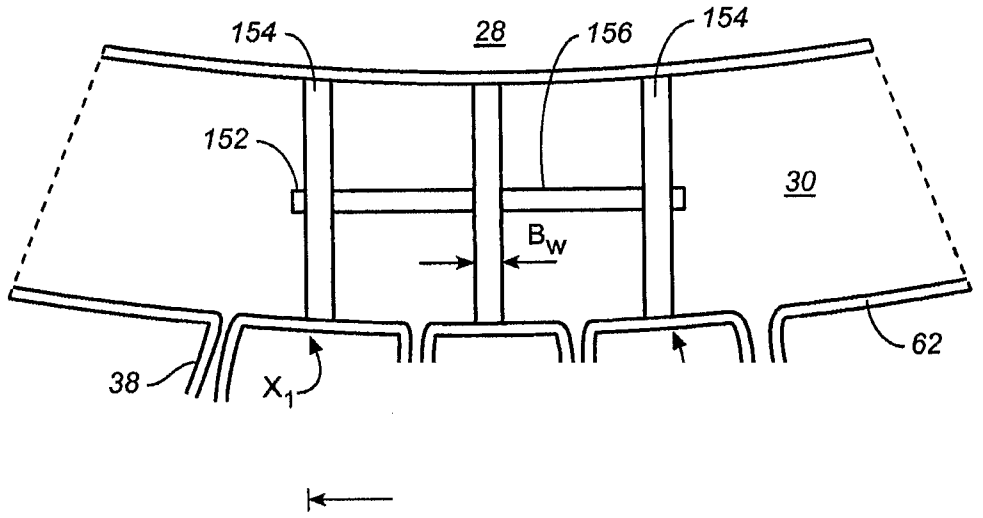


FIG. 8H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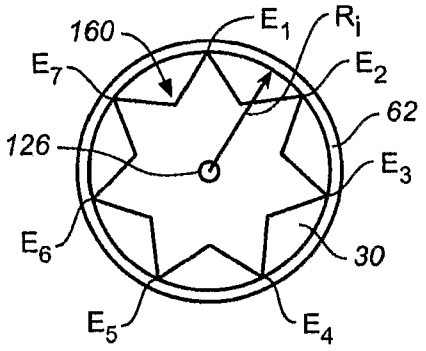
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FIG. 9B

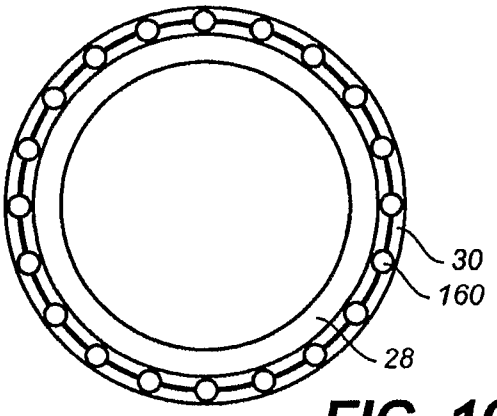


FIG. 10A

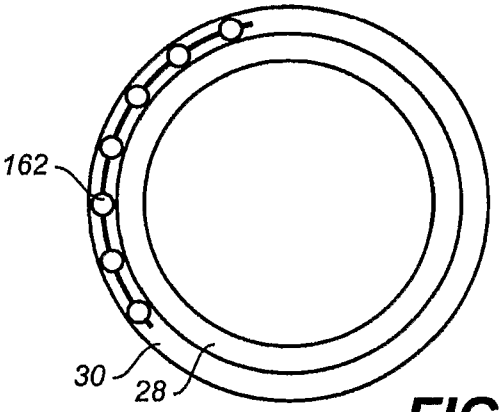


FIG. 10B

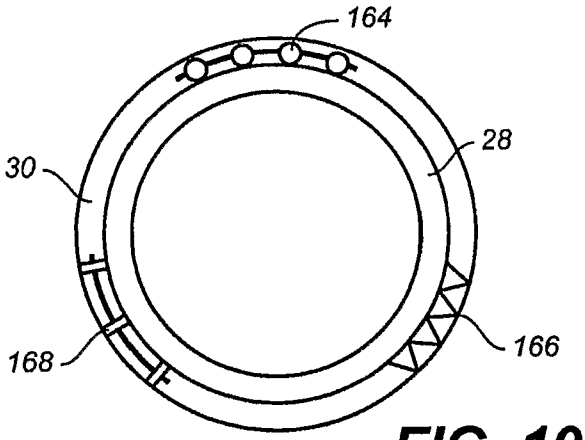


FIG. 10C

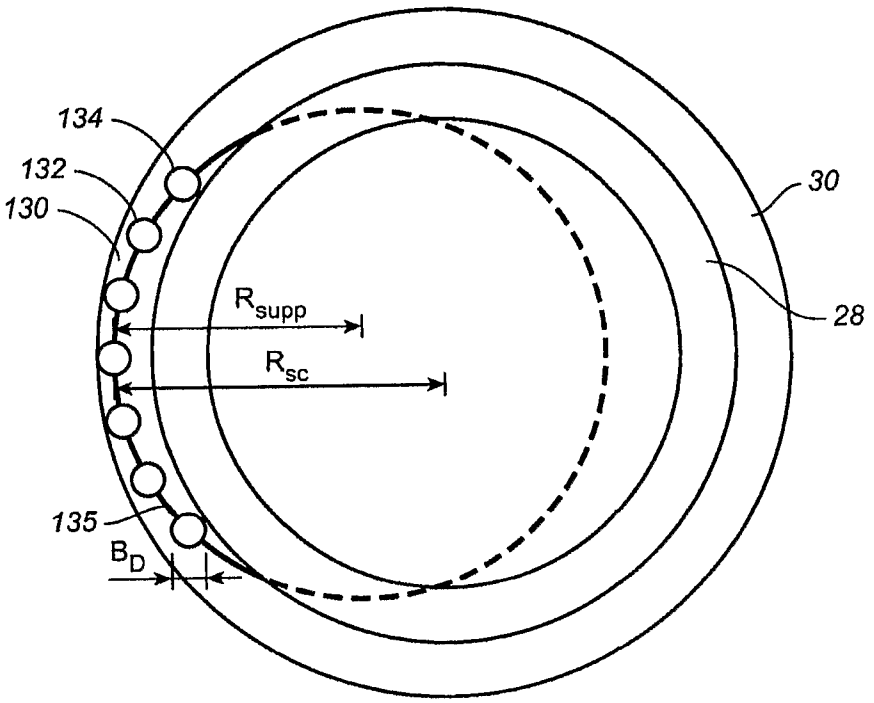
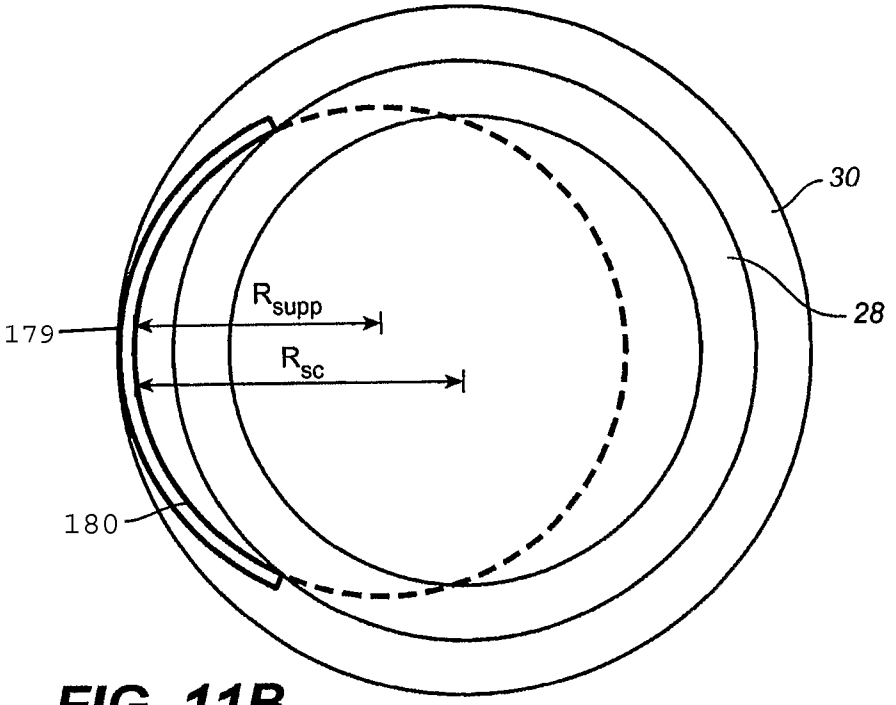


FIG. 11A



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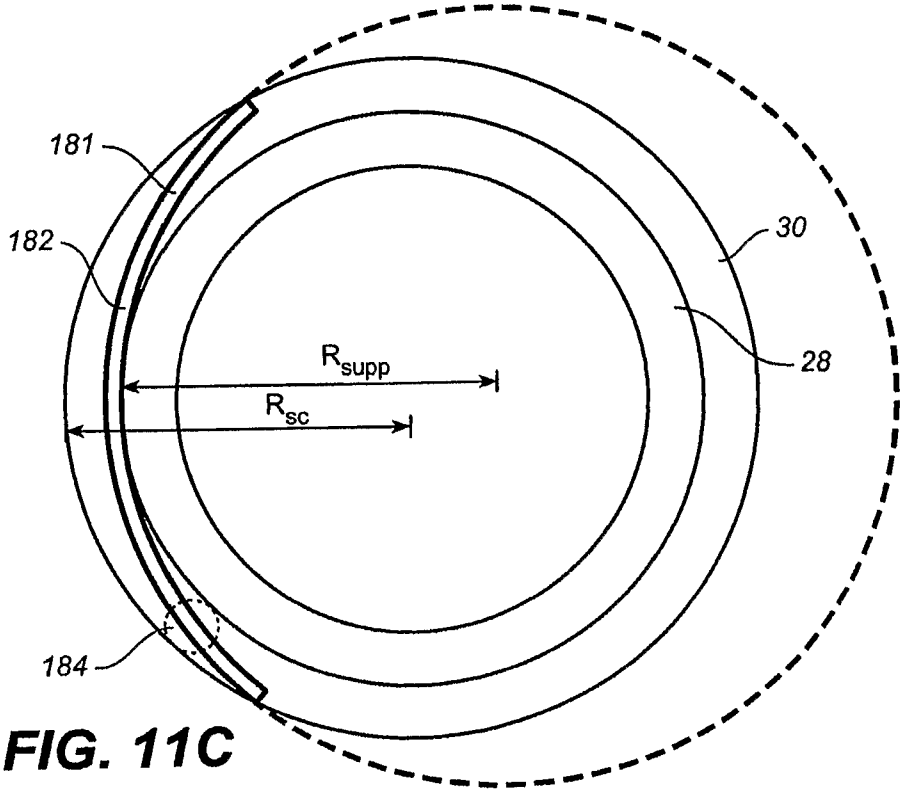


FIG. 11C

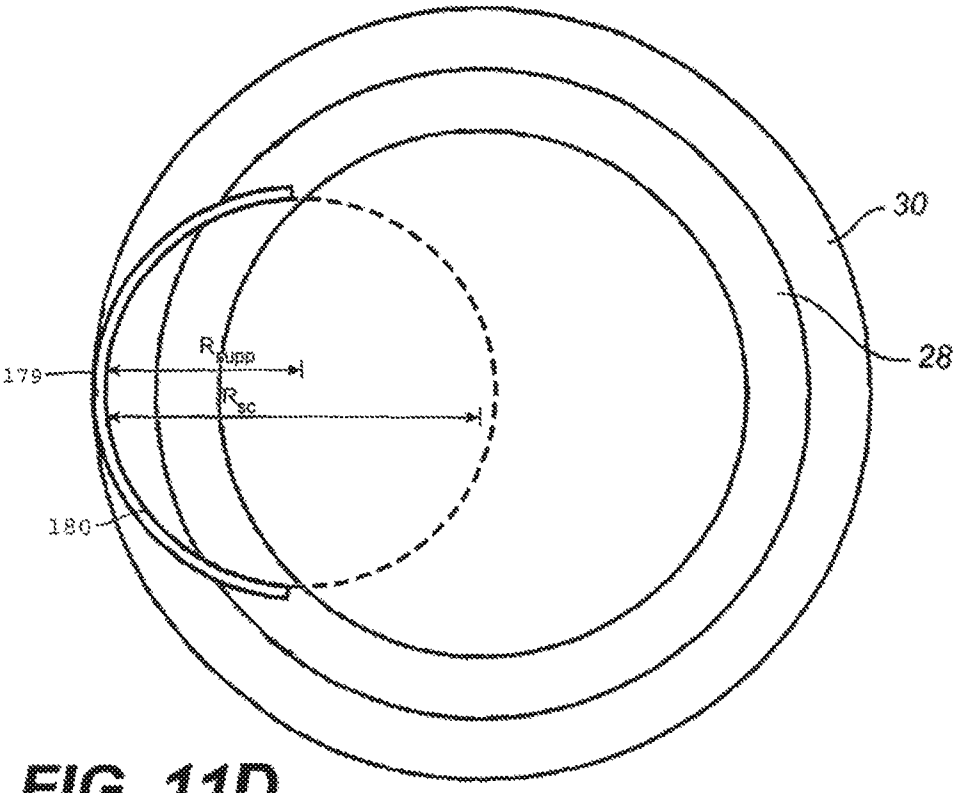


FIG. 11D

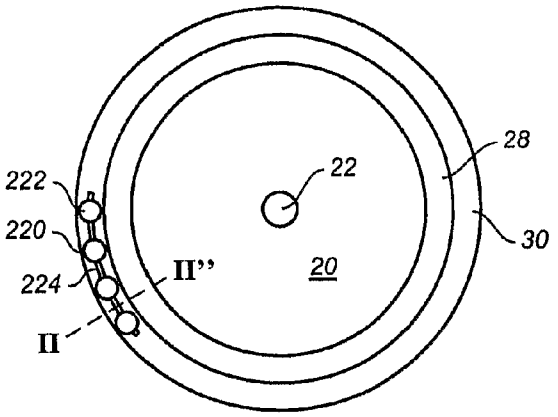
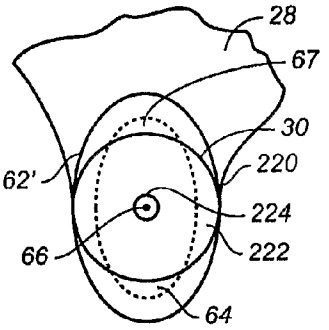


FIG. 12A



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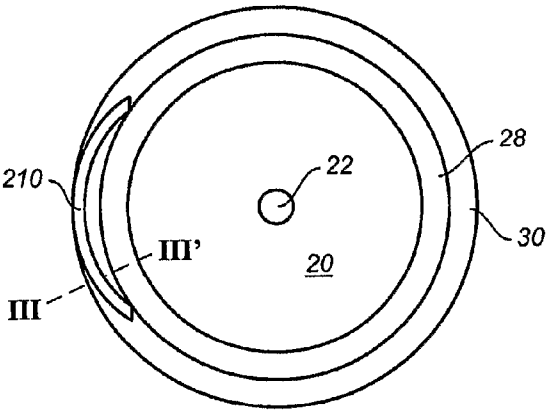

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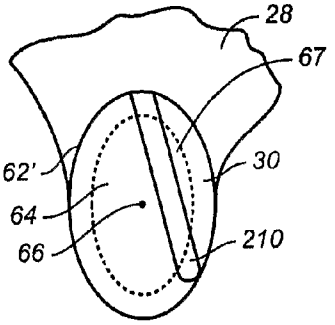

FIG. 12D

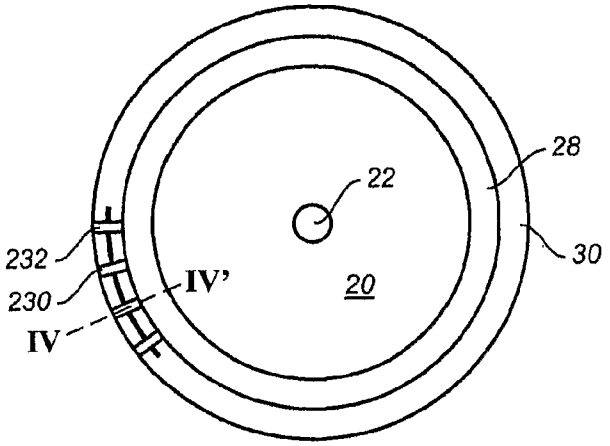

FIG. 12E

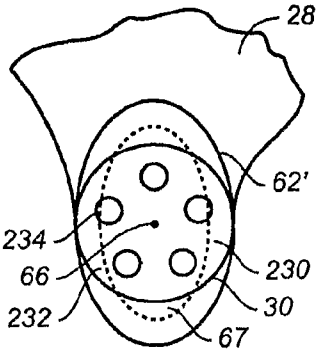

FIG. 12F

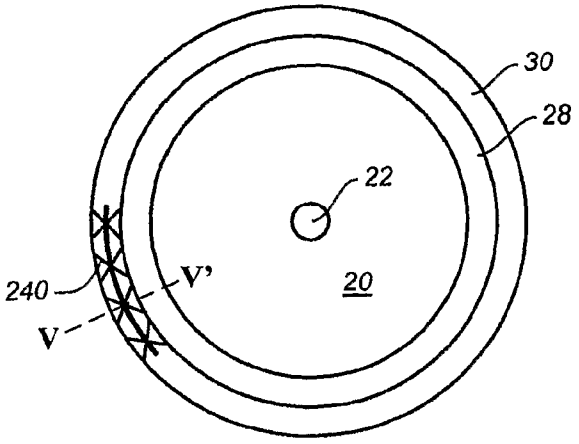

FIG. 12G

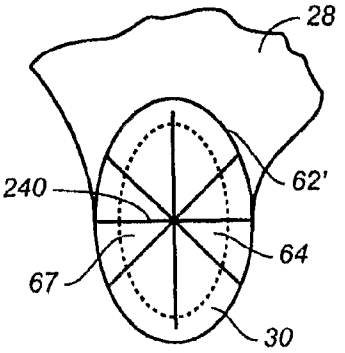

FIG. 12H

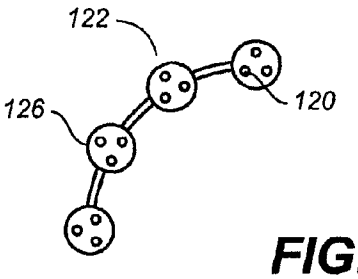

FIG. 13

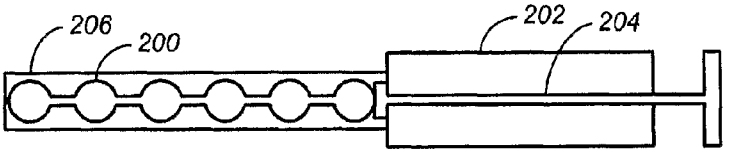

FIG. 14A

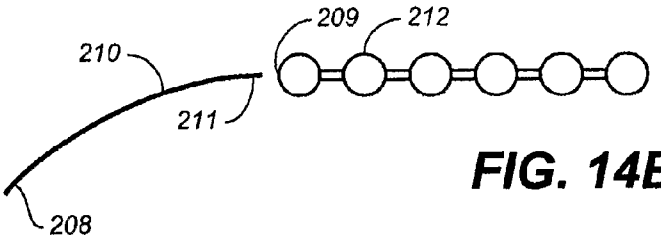

FIG. 14B

FIG. 14C

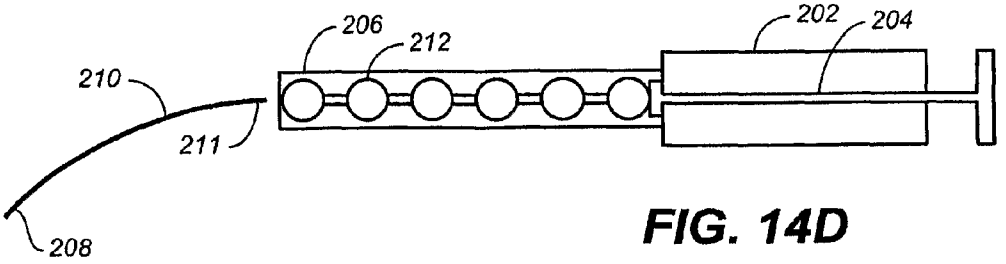

FIG. 14D

INTRAOCULAR IMPLANTS AND METHODS AND KITS THEREFOR

CROSS-REFERENCE TO RELATED APPLICATIONS

This application is a divisional of U.S. patent application Ser. No. 11/475,523, filed Jun. 26, 2006, the disclosure of which is incorporated herein by reference in its entirety.

FIELD

The devices, kits and methods described herein relate generally to intraocular pressure reduction. More particularly, the devices, kits and methods relate to intraocular implants implantable into Schlemm's canal that can reduce intraocular pressure without substantially interfering with fluid flow across Schlemm's canal.

BACKGROUND

Glaucoma is a potentially blinding disease that affects over 60 million people worldwide, or about 1-2% of the population. Typically, glaucoma is characterized by elevated intraocular pressure. Increased pressure in the eye can cause damage to the optic nerve which can lead to loss of vision if left untreated. Consistent reduction of intraocular pressure can slow down or stop progressive loss of vision associated with glaucoma. In addition, patients are often diagnosed with pre-glaucoma and ocular hypertension when they exhibit symptoms likely to lead to glaucoma, such as somewhat elevated intraocular pressure, but do not yet show indications of optic nerve damage. Treatments for glaucoma, pre-glaucoma and ocular hypertension primarily seek to reduce intraocular pressure.

Increased intraocular pressure is caused by sub-optimal efflux or drainage of fluid (aqueous humor) from the eye. Aqueous humor or fluid is a clear, colorless fluid that is continuously replenished in the eye. Aqueous humor is produced by the ciliary body, and then flows out primarily through the eye's trabecular meshwork. The trabecular meshwork extends circumferentially around the eye at the anterior chamber angle, or drainage angle, which is formed at the intersection between the peripheral iris or iris root, the anterior sclera or scleral spur and the peripheral cornea. The trabecular meshwork feeds outwardly into Schlemm's canal, a narrow circumferential passageway generally surrounding the exterior border of the trabecular meshwork. Positioned around and radially extending from Schlemm's canal are aqueous veins or collector channels that receive drained fluid. The net drainage or efflux of aqueous humor can be reduced as a result of decreased facility of outflow, decreased outflow through the trabecular meshwork and canal of Schlemm drainage apparatus, increased episcleral venous pressure, or possibly, increased production of aqueous humor. Flow out of the eye can be restricted by blockages or constriction in the trabecular meshwork and/or Schlemm's canal.

Glaucoma, pre-glaucoma and ocular hypertension currently can be treated by reducing intraocular pressure using one or more modalities, including medication, incisional surgery, laser surgery, cryosurgery, and other forms of surgery. In the United States, medications or medical therapy are typically the first lines of therapy. If medical therapy is not sufficiently effective, more invasive surgical treatments may be used. In other countries, such as those with socialized medical systems or with nationalized health care systems, surgery may be the first line of therapy if it is considered a more cost effective treatment.

A standard incisional surgical procedure to reduce intraocular pressure is trabeculectomy, or filtration surgery. This procedure involves creating a new drainage site for aqueous humor. Instead of naturally draining through the trabecular meshwork, a new drainage pathway is created by removing a portion of sclera and trabecular meshwork at the drainage angle. This creates an opening or passage between the anterior chamber and the subconjunctival space that is drained by conjunctival blood vessels and lymphatics. The new opening may be covered with sclera and/or conjuctiva to create a new reservoir called a bleb into which aqueous humor can drain. However, trabeculectomy carries both long and short term risks. These risks include blockage of the surgically-created opening through scarring or other mechanisms, hypotony or abnormally low intraocular pressure, expulsive hemorrhage, hyphema, intraocular infection or endophthalmitis, shallow anterior chamber angle, and others. Alternatives to trabeculectomy are actively being sought.

Bypass stents are also used to bridge a blocked trabecular meshwork. Stents can be inserted between the anterior chamber of the eye and Schlemm's canal, bypassing the trabecular meshwork. However, it is difficult to consistently and reliably implant a bypass stent from the anterior chamber into Schlemm's canal. The implant procedure is challenging and stents can become clogged and lose functionality over time. Others have inserted tubular elongated cylindrical hollow stents longitudinally into Schlemm's canal. Cylindrical hollow stents can be configured to allow circumferential fluid flow around the canal. These too can lose functionality over time as a result of occlusion or scarring.

Schlemm's canal is small, approximately 190-370 microns in cross-sectional diameter, and circular. Therefore, it can be difficult or expensive to design and manufacture hollow tubular stents of appropriate dimensions for use in opening Schlemm's canal. In addition, hollow tubular stents can be prone to failure and collapse or occlusion over time, as has been shown for cardiovascular stents. Hollow tubular stents incorporating thin walls are especially prone to failure. Further, the walls of tubular stents placed lengthwise along Schlemm's canal can have significant surface area contact with the trabecular meshwork and/or the collector channels, which can result in blockage of the meshwork or collector channels, substantially interfering with transmural flow across Schlemm's canal and into the eye's collector channels.

Therefore, easily manufacturable, minimally invasive devices for effective, long-term reduction in intraocular pressure are desirable. In addition, methods and kits incorporating such devices are desirable.

SUMMARY

Described here are devices, kits and methods for reducing intraocular pressure. The devices for reducing pressure within the eye comprise a support implantable circumferentially within Schlemm's canal that is configured to maintain the patency of at least a portion of the canal. The support occupies at least a portion of a central core of Schlemm's canal. The support does not substantially interfere with transmural flow across Schlemm's canal, and thereby utilizes the eye's natural drainage pathways. The support can be implanted into Schlemm's canal with minimal trauma to the eye.

The support generally comprises a biocompatible material. At least a portion of the support can be made from a biocompatible polymer, e.g., acrylics, silicones, polymethylmethacrylate, or a hydrogel. In addition, at least part of the support can be made from a biocompatible metal such as gold. In some variations, at least a portion of the support is made from a shape memory material. Suitable shape memory materials include shape memory polymers or shape memory alloys, such as nickel titanium alloys. If a shape memory material is used, the support can have a compressed state prior to and during implantation into Schlemm's canal, and an expanded state following implantation to open the canal.

In some variations, the support is at least partially made from a biocompatible, biodegradable polymer. The biodegradable polymer can be collagen, a collagen derivative, a poly(lactide); a poly(glycolide); a poly(lactide-co-glycolide); a poly(lactic acid); a poly(glycolic acid); a poly(lactic acid-co-glycolic acid); a poly(lactide)/poly(ethylene glycol) copolymer; a poly(glycolide)/poly(ethylene glycol) copolymer; a poly(lactide-co-glycolide)/poly(ethylene glycol) copolymer; a poly(lactic acid)/poly(ethylene glycol) copolymer; a poly(glycolic acid)/poly(ethylene glycol) copolymer; a poly(lactic acid-co-glycolic acid)/poly(ethylene glycol) copolymer; a poly(caprolactone); a poly(caprolactone)/poly(ethylene glycol) copolymer; a polyorthoester; a poly(phosphazene); a poly(hydroxybutyrate) or a copolymer including a poly(hydroxybutyrate); a poly(lactide-co-caprolactone); a polycarbonate; a poly(esteramide); a polyanhydride; a poly(dioxanone); a poly(alkylene alkylate); a copolymer of polyethylene glycol and a polyorthoester; a biodegradable polyurethane; a poly(amino acid); a polyetherester; a polyacetal; a polycyanoacrylate; a poly(oxyethylene)/poly(oxypropylene) copolymer; and blends and copolymers thereof.

The support can comprise an active agent. For example, a support can be coated or impregnated with an active agent. Alternatively, an active agent can be dispersed within the support, e.g., by filling a cavity within the support. The active agent can include a prostaglandin, a prostaglandin analog, a beta blocker, an alpha-2 agonist, a calcium channel blocker, a carbonic anhydrase inhibitor, a growth factor, an anti-metabolite, a chemotherapeutic agent, a steroid, an antagonist of a growth factor, or combinations thereof. The release of the active agent can be controlled using a time release system, e.g., by embedding or encapsulating the active agent with a time release composition.

In some variations, the support will be solid. In other variations, at least a portion of the support will be hollow or porous. The surface of the support may be smooth, rough, spiked, or fluted. In still other variations, at least part of the support will be made from mesh. The support can include at least one fenestration and one or more rod-like members.

In some variations, the support comprises at least two adjacent beads. Adjacent beads can have the same or different sizes and shapes, and can be made from the same or different materials. The bead shapes can be spherical, spheroid, ovoid, cylindrical, cuboid, cubical, conical, discoid, helical, or segments thereof. In some variations, there is a connector linking at least two adjacent beads together. If there is a connector, it can be rigid or flexible. If there is more than one connector, e.g., two connectors inserted between three beads, the connectors may be of the same or different lengths. The connectors can include the same or different material as the beads they connect. A connector can also function as a spacer configured to provide space between adjacent beads. In some variations, the support comprises at least two discs separated by, and connected with, a connector. The discs may include fenestrations. The connector may also comprise a guide wire over which a fenestrated bead can be threaded into the canal of Schlemm.

The support can extend approximately all the way around Schlemm's canal, if the support has a circumference approximately equal to the circumference of Schlemm's canal. Alternatively, the support can extend only about half way around the circumference of Schlemm's canal, or about a quarter way around the canal. In some variations, the support will extend less than a quarter circumference of Schlemm's canal. The support can be configured to contact the inner surface of the wall of Schlemm's canal at two, three or more points. In some variations, the support can be attached to tissue. The support may comprise a stiff arcuate member having a radius of curvature smaller or larger than that of Schlemm's canal.

In some variations, the support can be altered using electromagnetic radiation. For example, a laser having a wavelength absorbable by at least one localized portion of the support can be used to alter the support. In other variations, electromagnetic radiation can be used to release an active agent from the support. In still other variations, the support can be visually enhanced using fluorescence or phosphorescence emission. For example, the support can comprise a chromophore that fluoresces or phosphoresces upon excitation with a light source. In some variations, the emitted fluorescence or phosphorescence is in the wavelength range of about 300 nm to about 800 nm. In some variations, the support can comprise a chromophore that enhances postoperative monitoring of the support.

Kits for reducing intraocular pressure are also provided. The kits contain a support that can be implanted circumferentially within Schlemm's canal. The support is configured to maintain the patency of at least part of Schlemm's canal. The support occupies at least a portion of a central core of Schlemm's canal and does not substantially interfere with transmural flow across the canal. The kits also contain an introducer for implanting the support within the canal. In some variations, the kits include a positioning device for adjusting the support within the canal. In other variations, kits include instructions. In still other variations, the kits include an active agent. Some kits contain at least two supports. If more than one support is included, the kits can include at least two introducers for delivering the supports. Multiple supports within the same kit can have the same or different shape, size, or composition. Multiple supports within the same kit can be connected together or remain separate. In some variations, kits include a fixation device for attaching a support to tissue. In other variations, kits may include a system for visually enhancing the appearance of the support.

Methods for reducing intraocular pressure are also described. The methods include inserting a support circumferentially within Schlemm's canal. The support is configured to maintain the patency of at least part of the canal. The support occupies at least a portion of a central core of Schlemm's canal, and does not substantially interfere with transmural flow across the canal. In some variations, the methods also include dilating Schlemm's canal prior to insertion of the support. In still other variations, the methods comprise anchoring the support to tissue. The methods can include implanting at least two supports. If more than one support is implanted within a single eye, the multiple supports can be positioned circumferentially adjacent to each other or circumferentially opposed (i.e., positioned about 180° apart) to each other within Schlemm's canal. Multiple supports within one eye can be connected or remain separate. In some variations of the methods, the support is illuminated with a light source to visually enhance the position of the support. In

other variations of the methods, the support can be altered using electromagnetic radiation. For example, a laser absorbed by at least one localized portion of the support can be used to alter the support. The alteration can comprise the creation or enlargement of an aperture in the support. If electromagnetic radiation is used to alter a support, the alteration can occur before implantation or after implantation.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. **1** provides a partial cross-sectional side view of a normal human eye.

FIG. **2** provides a partial cross-sectional side view of a normal drainage path of fluid from the eye.

FIG. **3** shows a front view of normal fluid drainage from the eye.

FIG. **4**A shows an alternative front view of normal fluid drainage paths from the eye. FIG. **4**B shows a cross-sectional view along line I-I'.

FIG. **5**A provides a front view of an eye in which Schlemm's canal is narrowed or collapsed. FIG. **5**B shows a front view of a device including a support inserted into Schlemm's canal that allows transmural flow across the canal. FIG. **5**C illustrates an alternate design for a device inserted into Schlemm's canal that allows transmural flow across the canal.

FIG. **6**A shows side views of various element or bead configurations that can be used in the supports described herein. FIG. **6**B shows the corresponding front views of the element or bead configurations shown in FIG. **6**A. FIG. **6**C illustrates an element or bead having fenestrations.

FIG. **7**A illustrates a support having multiple juxtaposed beads. FIG. **7**B illustrates a support having multiple juxtaposed and connected beads. FIG. **7**C shows an alternate configuration of a support having multiple juxtaposed and connected beads. FIG. **7**D shows a support having multiple, spaced-apart but connected beads. FIG. **7**E illustrates beads threaded onto a connector.

FIGS. **8**A-B show side and front views, respectively, of a support having an open network structure. FIGS. **8**C-D show side and front views, respectively, of a support having a longitudinal zig-zag configuration that will contact the wall of Schlemm's canal at at least three points (labeled P_1, P_2, P_3). FIGS. **8**E-F show side and front views, respectively, of a support having a rod-like member with continuously fluted edges and fenestrations. FIGS. **8**G-H show side and front views, respectively, of another variation of a support having a rod-like member with continuously fluted edges.

FIGS. **9**A-B show expanded cross-sectional views of a support implanted within Schlemm's canal.

FIGS. **10**A-C illustrate various configurations of supports implanted into Schlemm's canal.

FIGS. **11**A-B and D illustrate configurations of supports having a smaller radius of curvature then Schlemm's canal. FIG. **11**C shows a support having a larger radius of curvature than Schlemm's canal.

FIG. **12**A illustrates a variation of a support traversing the center of the central core of Schlemm's canal. FIG. **12**B shows a cross-sectional view along line FIG. **12**C illustrates a variation of a support traversing the central core of the canal. FIG. **12**D shows a cross-sectional view along line FIG. **12**E illustrates a variation of a support that occupies the majority of the central core of the canal. FIG. **12**F shows a cross-sectional view along line IV-IV'. FIG. **12**G illustrates a variation of support having an open network that occupies a portion of the central core of the canal. FIG. **12**H shows a cross-sectional view along line V-V'.

FIG. **13** shows an illustrative example of a support that can be modified using electromagnetic radiation.

FIG. **14**A illustrates a syringe that can be used to insert a support into Schlemm's canal. FIG. **14**B illustrates a variation in which a support is threaded onto a guide element for insertion and positioning in Schlemm's canal. FIG. **14**C illustrates a cross-sectional view of a support having a central bore to accommodate a guide element. FIG. **14**D illustrates a variation in which a syringe and a guide element are used for insertion and positioning of a support in Schlemm's canal.

DETAILED DESCRIPTION

Described here are devices, kits and methods to reduce intraocular pressure by maintaining or restoring Schlemm's canal so that at least a portion of the canal is patent or unobstructed. The devices, kits and methods operate to keep Schlemm's canal from collapsing while not substantially interfering with the eye's natural drainage mechanism for aqueous humor, in which transmural fluid flow across Schlemm's canal occurs. The devices are implantable in Schlemm's canal with minimal trauma to the eye.

With reference to the figures, FIG. **1** shows a partial cross-sectional view of the anatomy of a normal human eye. Ciliary body **12** is connected to iris **18** and to lens **16** via zonular fibrils **14**. The anterior chamber of the eye **20** is bounded on its anterior (front) surface by cornea **24**. In the center of iris **18** is pupil **22**. Cornea **24** is connected on its periphery to sclera **26**, which is a tough fibrous tissue forming the white shell of the eye. Trabecular meshwork **28** is located on the outer peripheral surface of anterior chamber **20**. The trabecular meshwork extends 360° circumferentially around the anterior chamber. Located on the outer peripheral surface of meshwork **28** is Schlemm's canal **30**. Schlemm's canal extends 360° circumferentially around the trabecular meshwork. At the apex formed between iris **18**, meshwork **28** and sclera **26** is angle **32**. Conjunctiva **34** is a membrane overlaying sclera **26** and lining the inside of the eyelid (not shown).

FIG. **2** shows a partial cross-sectional view of flow of aqueous humor within and out of a normally functioning human eye. Aqueous humor is produced in ciliary body **12** and its path through and out of the eye is indicated by solid directional line **36**. The aqueous humor flows from ciliary body **12**, between lens **16** and iris **18**, through pupil **22** into anterior chamber **20**, across trabecular meshwork **28**, across Schlemm's canal **30**, into aqueous veins or collector channels (not shown) and finally into the bloodstream via conjunctival vasculature.

FIG. **3** shows a front view of normal flow of aqueous humor out of the eye. Aqueous humor enters anterior chamber **20** via pupil **22**. The fluid flows outwardly toward the periphery of the eye, with the general path of flow indicated by solid directional lines **36**. The fluid crosses trabecular meshwork **28** and traverses Schlemm's canal **30** to reach aqueous veins or collector channels **38**. There are typically 25-30 collector channels located in a human eye. Collector channels **38** are connected to vasculature **40**, whereby the drained aqueous humor enters the bloodstream. Although the direction of net or bulk fluid flow is depicted as radially outward by directional lines **36** from pupil **22** for simplicity, actual fluid flow in an eye may follow more varied paths.

Different fluid flow paths in and across Schlemm's canal are illustrated in FIGS. **4**A-B. FIG. **4**A shows a front view of an eye, and FIG. **4**B shows an expanded cross-sectional view along line I-I'. Circumferential (i.e., longitudinal) flow along and around circular canal **30** is depicted by directional lines **50**. Fluid that does not traverse canal **30** to reach collector

channels **38** may not be effectively drained from the eye. Examples of fluid flow paths that can effectively drain the eye are illustrated by directional lines **52**, **52'**, and **52"**. In each of these paths, fluid enters trabecular meshwork **28** along its inner peripheral surface **60** and exits the meshwork along its outer peripheral surface **62'**. Meshwork outer peripheral surface **62'** provides the inner peripheral surface or wall of Schlemm's canal **30**. Transmural fluid flow across Schlemm's canal involves two instances of transmural flow across walls or boundaries. First, fluid must flow from trabecular meshwork **38** through inner peripheral surface or wall **62'** of Schlemm's canal **30** to reach lumen **64** of the canal. Second, fluid must flow from lumen **64** through canal outer peripheral wall **62"** through apertures **38'** to enter collector channels **38**. Finally, the collector channels **38** feed the drained fluid into vasculature. Lumen **64** of canal **30** includes a central core region **67**. Thus, fluid flow from the eye differs from fluid flow in other vessels in the body where fluid need only flow longitudinally along the vessel, such as blood flowing through a vein.

Devices

Devices to reduce intraocular pressure comprising a support that can be implanted circumferentially in Schlemm's canal to maintain the patency of at least a portion of the canal are described here. The support occupies at least a portion of a central core of Schlemm's canal and does not substantially interfere with transmural flow across the canal. By "maintain the patency" of at least a portion the canal, it is meant that the support operates to keep the canal at least partially unobstructed to transmural flow, such that fluid can 1) exit through the trabecular meshwork; 2) traverse the canal; and 3) drain via the collector channels. To maintain the patency of the canal, it is not necessary that the support leave the canal unobstructed in regard to circumferential flow. By "does not substantially interfere" with transmural flow, it is meant that the support does not significantly block either fluid outflow from the trabecular meshwork or fluid outflow to the collector channels. In many variations, the support allows between about 0.1 and about 5 microliters per minute aqueous outflux from the eye through the trabecular meshwork and collector channels. The "central core of Schlemm's canal" refers to the region around the cross-sectional center of the canal in the interior space of the canal lumen, i.e., not on the periphery of the canal. Therefore, a device that occupies at least a portion of a central core of Schlemm's canal can traverse at least a portion of the canal's lumen.

Therefore, devices described here need not comprise an open-ended tubular support placed longitudinally along Schlemm's canal, i.e., the devices and supports can be non-tubular. A longitudinal, open-ended tubular support can enable longitudinal flow along the canal. However, even if fluid can flow longitudinally (i.e., circumferentially) along Schlemm's canal, the eye may not be effectively drained unless the fluid eventually traverses the canal. That is, transmural fluid flow across two boundaries must occur: 1) fluid must flow from the trabecular meshwork through a canal inner wall coincident with an outer peripheral boundary of the trabecular meshwork to reach the canal lumen; and 2) fluid must flow from the canal lumen through apertures in the canal outer peripheral wall to reach the connector channels. The collector channels are then able to further disperse the fluid and complete the natural draining process. A tubular support inserted longitudinally into the canal can have significant surface area overlap with surfaces of the canal such that transmural flow across the canal may be significantly impeded. A longitudinal tubular support placed in Schlemm's canal may block flow into the canal from the trabecular meshwork and block flow out of the canal into the collector channels.

Devices described herein for treating elevated intraocular pressure include a support that is implanted within Schlemm's canal. In many instances, the device will reduce the intraocular pressure by 1-40 mm Hg, for example by at least 2 mm Hg. In other instances, the device will reduce intraocular pressure by at least 4 mm Hg, or at least 6 mm Hg, or at least 10 or 20 mm Hg. In still other instances, the device will operate to bring the intraocular pressure into the range of about 8 to about 22 mm Hg. The support can be configured in a variety of ways to at least partially prop open Schlemm's canal thereby maintaining its patency without substantially interfering with or impeding transmural fluid flow across Schlemm's canal. In some variations, the support may interfere with or block longitudinal flow along or around the canal. In many instances, the support will be contained entirely within Schlemm's canal. In some variations the support will be implanted within the canal, but may extend partially beyond Schlemm's canal, e.g., into the trabecular meshwork.

In some variations, a support to maintain at least partial patency for Schlemm's canal to enable fluid flow between an inner wall of the canal and an outer wall of the canal can comprise elements or structures such as bead-like elements or beads, which can be connected together, e.g., as a string of beads. Individual elements or beads or a connected group of elements or beads can be inserted directly into Schlemm's canal. A more detailed description of supports incorporating elements or beads is provided below.

FIG. **5**A illustrates a front view of an eye having a narrowed or collapsed Schlemm's canal **30**, where canal outer peripheral wall **62"** is very close to canal inner peripheral wall **62'**. Although Schlemm's canal **30** is depicted in FIG. **5**A as being uniformly narrow around the entire circumference of canal, it is possible that only a portion of Schlemm's canal is narrowed or collapsed. When Schlemm's canal is collapsed or narrowed, net efflux of aqueous from the anterior chamber to the collector channels **38** is diminished, thereby increasing intraocular pressure. As a result, the risk of pre-glaucoma, ocular hypertension, or glaucoma can increase.

FIG. **5**B illustrates an example of a device **70** inserted into Schlemm's canal **30** through incision site **74**. Device **70** in this example is positioned to one side of incision site **74**. Device **70** includes support **72** that is configured to keep Schlemm's canal at least partially open to transmural fluid flow across both canal inner wall **62'** and canal outer wall **62"** to reach collector channels **38** via apertures **38'**. In the example shown in FIG. **5**B, support **72** includes elements or beads **76** connected with connectors **78**. In this variation, the distance between canal inner wall **62'** and outer wall **62"** is approximately determined by the cross-sectional dimension of support **72**, which is in turn determined by the largest cross-sectional diameter of the beads **76**. Therefore, circumferential (i.e., longitudinal) fluid flow around and along the canal **30** indicated by directional line **50** may be inhibited by the insertion of support **72** into the canal. However, transmural flow across both walls or boundaries of the canal indicated by directional lines **52**, **52'**, **52"** is enhanced by support **72** and fluid is able to reach collector channels **38** and be drained from the eye. As a result, support **72** can effectively reduce intraocular pressure by utilizing the eye's natural drainage mechanism. Incision **74** need only be large enough to accommodate the diameter of beads **76**, so that trauma to the eye is minimized. Beads can have cross-sectional dimensions in the range from about 50 microns to about 500 microns. Insertion of beads having relatively small cross-sectional diameters

(e.g., about 50 microns) into Schlemm's canal open the canal less than the normal cross-sectional diameter of the canal, which is about 190 to about 370 microns, but still can maintain the patency of the canal. Insertion of beads having relatively large cross-sectional diameters (e.g., greater than about 300 microns) can open the canal as large as or larger than the canal's normal cross-sectional diameter and also can operate to stretch the trabecular meshwork. Stretching the trabecular meshwork may further enhance drainage.

FIG. **5**C illustrates an alternate configuration of a device **80** inserted into Schlemm's canal **30** through incision site **84**. Device **80** includes support **82** that extends to both sides of incision site **84**. Support **82** includes elements or beads **76** connected with connectors **88** and **88'**. In this example, connector **88'** is of a different length than connectors **88**. As in FIG. **5**B, beads **76** may impede circumferential (i.e., longitudinal) fluid flow around and along canal **30** indicated by directional line **50**. However transmural flow across the canal is enhanced by support **82** that maintains patency across the canal and allows fluid to reach collector channels **38**. If the beads are fenestrated or comprise rough, spiked, or fluted perimeters, then circumferential fluid flow through or around the beads may also occur.

Elements or beads used in a support may be hollow and closed structures, open structures, solid structures, porous structures, or any combination thereof, and may be of any suitable shape. FIGS. **6**A and **6**B illustrate side and front views, respectively, of exemplary elements or beads that may be used in the supports described here. As shown, solid **90** or hollow **91**, spherical **90**, spheroid **92**, ovoid **93**, conical **94**, disk-shaped **95**, polyhedral **96**, rod-like **97**, or beads with fluted edges **98**, rough edges, **89**, or spiked edges **88** may be used. In some instances, it may be desired to round corners or edges of the beads. As illustrated in FIG. **6**C, elements or beads **76** may include fenestrations **99**, **99'**. Fenestrations may have any suitable cross-sectional shape, such as round or quadrilateral. Although a disc-shaped bead **76** is shown in FIG. **6**C, any shape of bead can be fenestrated.

As illustrated in the variations shown in FIGS. **7**A-E, two or more beads **76** in a support may be adjacent to each other. Adjacent beads may be juxtaposed (FIG. **7**A), connected and juxtaposed (FIGS. **7**B and **7**C), or connected together with connectors **100**, **100'** to form intervals between beads (FIG. **7**D). In addition, beads may be threaded onto a connector **101** (FIG. **7**E). Multiple beads used in a single support may have the same or different shapes, and may be made of the same or different materials.

Junctions **102** between beads as shown in FIG. **7**B can be made using any suitable technique, such as by using an adhesive, chemical bonding, mechanical interlocking, or welding. Beads may also be juxtaposed and connected as shown in FIG. **7**C by threading onto a guide element **104**. Guide element **104** can comprise a fiber, a suture, a guide wire, a fixture, or the like. The beads can be fixed in a juxtaposed configuration on a guide element, e.g., by knotting ends of the fiber or by providing other end-blocking devices **106**, such as clips, caps, protrusions, or the like on ends **108** of element **104**. Any or all of the beads can be attached to guide element **104**, e.g., beads occupying end positions may be attached to element **104** and function as blocking beads to keep beads from sliding off ends **108** of element **104**. Alternatively, beads may slide along element **104**. Guide element **104** can be flexible, such as thin polymer threads, such as a suture, or metal wires. Alternatively, element **104** can be flexible but fixable, such as one or more shapeable metal wires that can be bent into a desired position and maintain that position against some amount of external stress or pressure. In other variations, guide element **104** can be rigid, e.g., a molded polymeric piece or a stiff metal piece.

As shown in FIG. **7**D, multiple connectors **100**, **100'** may be used in a single support, with at least one connector inserted between adjacent beads **76**. If multiple connectors are used, they may be of the same or different lengths. In addition, multiple connectors within the same support may be made of the same or different materials, and the connectors may be made of the same or different materials than the beads. Discrete connectors **100**, **100'** can be inserted between beads **76** and attached to adjacent beads using any suitable method including using adhesives, chemical bonding, welding, mechanical interlocking, knots, or any combination thereof. In some variations, connectors **100**, **100'** between beads can be configured to function as spacers between individual beads. As illustrated in FIG. **7**E, beads **76** can also be threaded onto a connector **101**. If the beads are threaded onto a connector, the beads can be maintained in fixed positions along the connector **101** by any suitable method, including using adhesives, chemical bonding, welding, clips, protrusions on the connector, mechanical interlocking locking between a connector and a bead, knots, or any combination thereof. Alternatively, some or all beads may slide along connector **101**. Connectors **100**, **100'**, **101** can be flexible, such as thin polymer threads or metal wires. Connectors **100**, **100'**, **101** can also be flexible but fixable, such as shapeable metal wires. Alternatively, connectors **100**, **100'**, **101** may be rigid, such as molded polymeric connectors or stiff metal connectors.

Supports of the devices described here need not contain beads. For example, a support can be a unitary structure of fixed or variable length. Supports can be solid, hollow, or porous, or any combination thereof. For example, a support can be partially solid and partially hollow. Examples of support configurations are shown in side view and front view in FIGS. **8**A-F. As illustrated in FIG. **8**A-B, a support can have an open network structure. Such a support can be fabricated out of shapeable metal wires, for example. The support illustrated in FIGS. **8**A-B will have minimal surface area contact with the walls of Schlemm's canal, i.e., only point contacts at the end of wires or fibers **170**. Alternatively, a support having an open network structure can be at least partially made from a mesh or foam. The mesh or foam can be made of any suitable material, e.g., metal or plastic. As shown in FIGS. **8**C-D, the support can have a sinusoidal or zig-zag configuration extending along a selected length of Schlemm's canal. For the example shown in FIG. **8**C, the support will contact the wall of Schlemm's canal at at least three points, labeled P_1, P_2, and P_3, after implantation. In FIGS. **8**E-H, examples of rod-like supports having fluted edges are shown. In FIGS. **8**E-F, fluted edges **110** extend longitudinally along sides **112** between ends **114** of the support to form structures **116**. Structures **116** can include fenestrations **113**. The support can include central bore **117**. In FIGS. **8**G-H, fluted edges **110'** extend along sides **112'** to form structures **116'**. Structures **116'** have serrated outer surfaces **115'** extending between ends **114'**. The support can include central bore **117'**. In the variations illustrated in FIGS. **8**E-H, the support may contact the canal walls at at least four points. In some variations, the support is adjustable.

A common characteristic of the support configurations described here is that they need not have continuous or extensive contact with a wall of Schlemm's canal. Indeed, many of the described devices and structures have minimal tangential, periodic, or sporadic contact with the wall. The surface of the support can be rough, smooth, spiked or fluted. As the example shown in FIGS. **8**A-B shows, some supports only

have point contacts with the canal wall. For the supports shown in FIGS. **5**B-C, the rounded beads of each of the supports make only tangential contact with the canal wall. Bead shapes can be selected or designed to have minimal surface area contact with canal walls, e.g., beads **98** having fluted edges as shown in FIGS. **6**A-B may have low surface area contact with canal walls. In addition, supports having widely spaced apart beads, e.g., by connectors illustrated in FIGS. **7**D-E that can function to space beads at desired intervals to reduce contact with canal walls yet operate to keep the canal open. As illustrated above with respect to FIGS. **8**C-D, in some variations, the support contacts the interior wall of the canal at at least two points; or at at least three points.

Expanded cross-sectional views of a support **152** implanted circumferentially in Schlemm's canal are provided FIGS. **9**A-B. The fraction of canal wall surface area in contact with a support can be estimated by viewing the inside of Schlemm's canal as a slightly arcuate cylinder C having length L, extending circumferentially from a first end X_1 to a second end X_2 of support **152**, and inside radius R_i. In some variations, the support contacts less than 0.1% or less than 1% of the surface area of the cylinder C as described above. In other variations, the support contacts less than 10% of the surface area of C. In still other variations, the support contacts less than 30% of the surface area of C. For example, the support **152** shown in FIGS. **9**A-B contacts the canal wall **62** only at bead outer peripheral edges at E_1-E_7, along a distance of the bead width B_W. There is no contact with the canal walls where connectors **156** space apart beads **154**, and no contact in fluted regions **160** of beads **154**. The design feature of minimal support contact with canal walls allows a support to maintain patency of the canal without substantially interfering with transmural flow across the canal. If a substantial portion of the surface area of the inner periphery of the canal adjacent to the trabecular network or of the surface area of the outer periphery of the canal where the collector channels are located is blocked, effective fluid flow across the canal may be impaired.

Supports can have variable lengths and thicknesses. For example, the length of supports using beads can be tuned by varying the number, type, or spacing of beads, or any combination thereof. The thickness of a support can be increased by adding one or more beads having larger dimensions. Unitary supports can also be built with varying lengths, or with adjustable (e.g., trimmable) dimensions. For example, for a support made of shapeable metal having a sinusoidal or zig-zag configuration as shown FIGS. **8**C-D, a cross-sectional dimension **117** of the support can be decreased or increased by apply tension along dimension **119**. As illustrated in FIG. **10**A, a support **160** can extend essentially around the entire circumference of Schlemm's canal **30**. Alternatively, a support can extend approximately half way around the circumference of the canal (not shown). As shown in FIG. **10**B, a support **162** can extend less than half way around the canal. As shown in FIG. **10**C, a support **164** can extend a quarter or less of the circumference around the canal. In addition, more than one support **164**, **166**, **168** can be inserted into a single Schlemm's canal. If multiple supports are inserted into a single canal, they can be of different shapes, lengths, materials or sizes.

A support can be configured such that it will open the canal beyond a maximum cross-sectional dimension of the support itself. For example, as illustrated in FIG. **11**A, device **130** comprising support **132** is inserted into Schlemm's canal **30**. Support **132** comprises beads **134** which have a maximum cross-sectional dimension B_D. Support **132** comprises a stiff arcuate element **135** with a radius of curvature R_{supp} smaller than the radius of curvature of Schlemm's canal R_{SC}. The smaller, fixed radius of curvature R_{supp} of arcuate member **135** urges canal **30** to open more than B_D. In other variations shown in FIGS. **11**B and **11**D, support **179** comprises an arcuate member **180** without beads having a radius of curvature R_{supp} that is less than the radius of curvature R_{SC} of the canal. Member **180** is sufficiently stiff to urge the canal open. In another variation shown in FIG. **11**C, support **181** comprises an arcuate member **182** having a radius of curvature R_{supp} larger than that of Schlemm's canal R_{SC}. Member **182** is also sufficiently stiff to urge the canal open. Arcuate members **135**, **180** and **182** can comprise a shape memory material such as Nitinol, for example. As indicated in FIG. **11**C, support **181** can include beads **184**. To urge open the canal, the radius of curvature R_{supp} of an arcuate members can be about 10%, 20%, 30%, 40%, or 50% or smaller or larger than that of Schlemm's canal R_{SC}. For example, an arcuate member can have a radius of curvature of about 3 mm to about 8 mm. In some variations, the radius of curvature of an arcuate member R_{supp} in a support is about 3 mm, or about 4 mm, or about 5 mm. In other variations, the radius of curvature R_{supp} of an arcuate member in a support is about 6 mm, or about 7 mm, or about 8 mm.

The supports described here occupy at least a portion of a central core of Schlemm's canal. The central core of Schlemm's canal is the region around the cross-sectional center of the canal in the interior space of the canal lumen. A support that occupies at least a portion of the central core of the canal can traverse at least a portion of the canal lumen. For example, some variations of supports can traverse the cross-sectional center of the canal at at least one point. Referring to FIG. **12**A, a front view of a support **220** having beads **222** connected with connectors **224** is provided. FIG. **12**B shows an expanded cross-sectional view along line II-II'. Support **220** occupies a portion canal central core **67** in canal lumen **64**. Trabecular meshwork **28** is shown adjacent to canal **30**. In this variation, support **220** traverses the cross-sectional center **66** of the canal. In other variations, supports can traverse the lumen of the canal off-center, e.g., appearing as a chord across the canal lumen in cross-section. Referring to FIG. **12**C, a front view of an arcuate support **210** is shown. FIG. **12**D shows an expanded cross-sectional view along line III-III'. Support **210** traverses and occupies a portion of central core **67** in lumen **64** of canal **30** without passing through canal center **66**. In some variations, the support can occupy the majority of the central core of the canal. Referring to FIG. **12**E, a front view of support **230** comprising disc-like beads **232** is shown. A cross-sectional view along line IV-IV' is shown in FIG. **12**F. As illustrated in FIG. **12**F, bead **232** with fenestrations **234** occupies the majority of central core **67** of canal **30**. In other variations, the support occupies only a small portion of the central core of the canal. For example, in FIG. **12**G, a front view of a support **240** having an open network structure is shown. A cross-sectional view along line V-V' is shown in FIG. **12**H.

A support can made of a variety of different materials. In general, the support should comprise a biocompatible material, such as a biocompatible polymer, ceramic or ceramic composite, glass or glass composite, metal, or combinations of these materials. Examples of biocompatible metals include stainless steel, gold, silver, titanium, tantalum, platinum and alloys thereof, cobalt and chromium alloys, and titanium nickel alloys such as Nitinol. Examples of biocompatible polymers include high density polyethylene, polyurethane, polycarbonate, polypropylene, polymethylmethacrylate, polybutylmethacryate, polyesters, polytetrafluoroethylene, silicone, polyvinyl alcohol, polyvinyl pyrrolidone, polyvinyl chloride, ethyl vinyl acetate, collagen, collagen derivatives,

flexible fused silica, polyolefins, NYLON® polymer, polyimide, polyacrylamide, fluorinated elastomers, and copolymers and blends thereof. In addition, biocompatible hydrogels can be used in supports and devices described herein. As discussed in more detail below, biocompatible polymers may be biodegradable. A support can be made of a single material or a combination of materials. In some variations, a support made from a first material is coated with a second material, e.g., to enhance or improve its biocompatibility.

In some examples, the biocompatible polymer in a support will include a biodegradable polymer. Examples of suitable biodegradable polymers include collagen, a collagen derivative, a poly(lactide), a poly(glycolide), a poly(lactide-co-glycolide), a poly(lactic acid), a poly(glycolic acid), a poly(lactic acid-co-glycolic acid), a poly(lactide)/poly(ethylene glycol) copolymer, a poly(glycolide)/poly(ethylene glycol) copolymer, a poly(lactide-co-glycolide)/polyethylene glycol) copolymer, a poly(lactic acid)/poly(ethylene glycol) copolymer, a poly(glycolic acid)/poly(ethylene glycol) copolymer, a poly(lactic acid-co-glycolic acid)/poly(ethylene glycol) copolymer, a poly(caprolactone), a poly(caprolactone)poly (ethylene glycol) copolymer, a polyorthoester, a poly(phosphazene), a poly(hydroxybutyrate) or a copolymer including a poly(hdroxybutyrate), a poly(lactide-co-caprolactone), a polycarbonate, a poly(esteramide), a polyanydride, a poly (dioxanone), a poly(alykylene alkylate), a copolymer of polyethylene glycol and a polyorthoester, a biodegradable polyurethane, a poly(amino acid), a polyetherester, a polyacetal, a polycyanoacrylate, a poly(oxyethylene)/poly(oxypropylene) copolymer, and blends and copolymers thereof.

At least a portion of the support can be made from a shape memory material. For example, shape memory alloys, e.g. a nickel-titanium alloy can be used. In addition, shape memory polymers, e.g., polymers made from copolymerizing monomers oligo(e-caprolactone) dimethacrylate and n-butyl acrylate or polymers based on styrene acrylate, cyanate ester and epoxies, can be used. If a shape memory material is used in the support, the support can have a compressed state prior to and during implantation, and an expanded state following implantation. The use of a compressed state support comprising a shape memory material can allow for a smaller incision and facilitate insertion into a narrowed or compressed Schlemm's canal. Once implanted, the support can be expanding using any suitable method, e.g., thermally activated by body heat or an alternate heat source, to adopt an expanded state, thereby opening the canal.

The support can include an active agent, such as a pharmaceutical. Active agents can include prostaglandins, prostaglandin analogs, beta blockers, alpha-2 agonists, calcium channel blockers, carbonic anhydrase inhibitors, growth factors, such as tissue growth factors and vascular endothelial growth factors, anti-metabolites, chemotherapeutic agents such as mitomycin-C,5-fluorouracil, steroids, antagonists of growth factors such as antagonists of vascular endothelial growth factors, or combinations thereof. The active agent can be provided as a coating on at least a portion of a support. The active agent can be delivered throughout the eye by dissolution or other dispersal mechanisms. Alternatively, at least a portion of the support can be impregnated with the active agent. In other embodiments, the active agent can be dispersed within at least a portion of the support. For example, a cavity in the support can be filled with the active agent.

The delivery of the active agent can be controlled by time-release. For example, the portion of the support containing the active agent can include a time release coating or time release formulation designed to gradually dissipate the active agent over a certain period of time. Biodegradable coatings and formulations for time-release of active agents are known in the art. In some variations, the support can comprise multiple layers, where the layers each comprise an active agent. For example, support layers can be used to release a series of different agents, or a series of doses of the same agent. Such layers can be part of a coating applied to a support, or part of a support body. In addition, the support can comprise biodegradable layers containing no active agent that can be applied or interspersed between other layers to further control delivery of active agents to the eye.

In some variations, it will be desirable to change or alter the support using electromagnetic radiation. For example, at least a portion of a support can be fenestrated, perforated, bent, shaped or formed using a laser to enhance intraocular pressure reduction. As illustrated in FIG. **13**, predetermined localized portions **120** of support **122** can be designed to absorb light of a certain wavelength or wavelength range. Preferential absorption can be achieved by material selection and/or by doping with chromophores. Upon irradiation with sufficient energy at the selected wavelength or wavelength range, the patterned regions **120** will ablate or melt, leaving new or enlarged perforations or indentations in the support. For example, a pulsed titanium sapphire laser operating between about 750 and about 800 nm can be used to ablate gold regions. If beads **126** in support **120** are hollow, then after irradiation and ablation, features **120** will become fenestrations. The fenestrations can be created to make support **122** more porous in nature or to allow release of an active agent from within a support, e.g., from within beads **126**. Alternatively, it is possible to use a mask in combination with electromagnetic radiation to alter a support, such as by patterning or machining. The modification of a support using electromagnetic radiation can be carried out prior to or subsequent to insertion.

In some variations, the visual appearance of the support can be enhanced under certain conditions to facilitate placement or to monitor the position or condition of the support. Visual enhancement can be achieved by incorporating into or onto the support chromophores that fluoresce or phosphoresce upon excitation with a light source. Chromophores can also assist a clinician in verifying the position of the support postoperatively using a gonioscope, for example. Light sources can include lasers, lamps, and light emitting diodes. In some instances, transmission or absorption filters may be used to select the wavelength of the excitation source or to detect or view emission. Emission from a support capable of visual enhancement may be in the wavelength range of about 300 nm to about 800 nm. The chromophores can be an integral component of the material making up the support, doped into support material, or coated or sprayed onto the support. Visually-enhancing chromophores can be applied on a temporary basis, or on a permanent basis. An example of a suitable chromophore is fluorescein, which can be excited with any laser or lamp emitting at about 400 to about 500 nm. In addition, phosphorus-based chemiluminescent or photoluminscent pigments can be used, which can be selected to absorb at various wavelengths across the visible spectrum.

In some variations, the support may be capable of being attached to tissue. For example, the support may include a hook, loop, clip, extension, or the like that may be easily attached to tissue. The support may also be attached to tissue using sutures or adhesives. The support may be attached to tissue using more than one attachment method, e.g., suturing may be used in combination with a loop, or an adhesive may be used in combination with a hook. In other variations, the support may be allowed to self-position in Schlemm's canal.

In still other variations, the support may be mobile within Schlemm's canal.

Kits

Kits for reducing intraocular pressure are provided, where the kits contain at least one support that can be implanted circumferentially within Schlemm's canal configured to maintain the patency of at least a portion of Schlemm's canal. The support occupies at least a portion of a central core of Schlemm's canal and does not substantially interfere with transmural flow across the canal. The kits also provide an introducer or delivery device for implanting the support in the canal. The support and introducer are provided in packaged combination in the kits. The kits can also include instructions for use, e.g., for implanting and inspecting the support.

The introducer can be inserted into the eye and is capable of implanting the support at the desired implantation position within Schlemm's canal. For example, an introducer may include a tubular cannula through which the support may be passed. In addition to a cannula, the introducer may include a tubular or solid pusher rod that can be used to push or advance the support into and/or around Schlemm's canal. Alternatively, a pusher rod or plunger can be used without a cannula to introduce a support into the canal. A support can be installed into the lumen of a cannula prior to insertion, the distal end of the cannula positioned at or near the desired support location, and the pusher rod operated from the proximal end to push the support distally out of the distal end of the cannula and into the canal. The cannula and/or the pusher rod may be flexible and small enough in diameter to extend at least partially around the canal. In some variations, a proximal end of a suture can be introduced into the canal via a cannula and the suture extended circumferentially around the canal. A distal portion of the suture can be connected to the support and force applied to the proximal end of the suture to pull the support into the canal. The support can then be positioned within the canal by pulling the suture in a distal or proximal direction. The suture can be used to anchor the support within the canal. In other variations, the support can be directly introduced into the canal using surgical forceps, or the like.

FIGS. **14**A-D illustrate additional variations for introducing a support into the canal. As shown in FIG. **14**A, a support **200** can be introduced into the canal using syringe **202** and plunger **204**. Syringe **202** has distal end **206** that can be at least partially inserted into or placed adjacent to an opening in the canal. Force in a distal direction is applied to plunger **204**, thereby pushing support **200** into the canal. Referring to FIGS. **14**B-C, distal end **208** of guide element **210** can be at least partially introduced into the canal. Guide element **210** can be a guide wire. Guide element **210** can be extended circumferentially along the canal to aid in positioning the support. Support **212** comprises central bore **218** capable of accommodating guide element **210** such that support **212** can be threaded onto guide element **210** and slidably positioned along the guide element. Once distal end **209** of support **212** is threaded onto guide element **210**, support **212** can be pushed in a distal direction along guide element **210** to insert support **212** into the canal. In some variations, support **212** can remain threaded onto guide element **210**, and guide element **210** can remain in the canal. In other variations, support **212** can be slid off distal end **208** of guide element **210**, and the guide element can be pulled in a proximal direction for removal. Referring to FIGS. **14**C-D, syringe **202** with plunger **204** can be used in combination with a guide element **210**. In this variation, distal end **208** of guide element **210** is inserted at least partially into Schlemm's canal. Guide element **210** can be extended circumferentially along the canal to aid in positioning the support. Support **212** has central bore **218** capable of accommodating guide element **210**. Proximal end **211** of guide element **210** is inserted into bore **218**. Plunger **204** is depressed in a distal direction to push support **212** into the canal and slide support **212** along element **210**. Guide element **210** can remain in the canal or be removed following insertion of the support. Supports **200**, **212** must be sufficiently resilient to withstand force encountered as they are pushed into the canal.

In some variations, a positioning device may be used with the introducer to position or adjust the support within the canal. A positioning device can include a rod, grippers, a clamp, a hook, or the like. In other variations, a device or system capable of dilating the canal to facilitate insertion of a support may be included in the kits, e.g., a syringe or other device capable of injecting fluid into the canal.

In some variations, the kits contain at least two supports. Multiple supports can be implanted within one eye or within multiple eyes. If the kits contain multiple supports, the kits may also contain multiple introducers. Alternatively, the same introducer may be used for implantation of multiple supports, especially if the multiple supports are being delivered to a single eye. If multiple supports are to be delivered with the same introducer, then the multiple supports can be preloaded into the introducer for sterility. If more than one support is included in a kit, the supports may be of different shapes, sizes, lengths, or materials. If the kits contain more than one support to be implanted into a single eye, the supports can be connected together.

The kits can comprise an active agent, such as a pharmaceutical agent. The active agent may be included as an integral part of the support, or may be supplied in kits for application to the support or to the eye during or after implantation. Examples of active agents that may be supplied as part of the kits include prostaglandins, prostaglandin analogs, beta blockers, alpha-2 agonists, calcium channel blockers, carbonic anhydrase inhibitors, growth factors, such as tissue growth factors or vascular endothelial growth factors, antimetabolites, chemotherapeutic agents such as mitomycin-C, 5-fluorouracil, steroids, antagonists of growth factors, such as antagonists of vascular endothelial growth factor, and combinations thereof.

The kits may contain a fixation device for attaching a support to tissue. Such a fixation device can include sutures, hooks, barbs, clips, adhesives, and combinations thereof. In addition, the kits may include a system for visually enhancing the support to facilitate viewing, positioning, and monitoring of a support. A system for visually enhancing the support can include a light source, a transmission or absorption filter, a mirror, a composition comprising a chromophore capable of fluorescing or phosphorescing that can be applied to the support, or any combination thereof. Chromophores can assist a clinician in verifying the position of the support postoperatively using a gonioscope, for example. The light source is capable of exciting a chromophore contained within or on the support such that the chromophore emits fluorescence or phosphorescence. The emission is preferably within the wavelength range of about 300 nm to about 800 nm. A suitable light source for such a system can comprise a laser, a light emitting diode, or a lamp. In some instances, transmission or absorption filters may be used to further select the wavelength range of the excitation source or view or detect emission from chromophores. One or more mirrors may be used to direct a light source or emitted light, or to view the support.

Methods

Methods for reducing intraocular pressure are also provided. In general, the methods comprise inserting a support circumferentially within Schlemm's canal, such that the support maintains the patency of at least a portion of the canal. The support occupies at least a portion of a central core of Schlemm's canal and does not substantially interfere with transmural flow across Schlemm's canal.

The methods can comprise inserting a support circumferentially into Schlemm's canal using an introducer and/or a positioning device. The introducer can include a cannula and a tubular or hollow pusher rod. The support can be installed in the lumen of the cannula at its distal end and the pusher rod can be inserted into the lumen of the cannula at its proximal end and extended distally to push the support into position in the canal. In some instances, the cannula and/or the pusher rod may be flexible and small enough in diameter to at least partially extend circumferentially around the canal. In some variations of the methods, a positioning device can be used in addition to an introducer. The positioning device can comprise a second rod, a gripper, a hook, a clamp, or the like. In some variations, the methods include illuminating a support with a light source to causes the support to fluoresce or phosphoresce, thus aiding the visual appearance of the support. The illuminating of the support can occur during or after implantation to inspect the support, e.g., to monitor its position, condition, or performance.

In some instances, the methods will also comprise dilating Schlemm's canal prior to insertion of the support. Dilation of the canal can be accomplished by injecting fluid into the canal. For example, a high viscosity fluid such as sodium hyaluronate, or other dilating fluids known in the art, can be used to dilate the canal.

The methods may include implanting more than one support into an eye. In some variations, the methods will include implantation of two or more supports circumferentially adjacent to each other within the canal, and in other variations, the methods will include implantation of supports circumferentially opposed to each other within the canal, e.g., two supports centered about 180° apart around the circumference of Schlemm's canal. Some variations of the methods can comprise connecting together multiple supports in a single eye.

In some variations, the methods can include anchoring the support to tissue surrounding Schlemm's canal. Anchoring the support to tissue can be accomplished in a variety of ways, e.g., by suturing, application of adhesives, installation of hooks, clips, or the like, or combinations thereof. In other variations, the methods can comprise selecting the size of the support such that the support fits securely into the canal by a friction fit. Examples of arcuate supports that can be implanted with a friction fit are illustrated in FIGS. **11**A-C.

The methods described here can also include altering the support using electromagnetic radiation. For example, a support can include regions capable of preferentially absorbing a certain wavelength range. When electromagnetic radiation of the appropriate wavelength range with sufficient energy is incident upon the support, material in the preferentially absorbing regions will melt or ablate, resulting in perforations or indentations in the support at those regions. For example, a pulsed titanium sapphire laser emitting at about 750 nm to about 800 nm incident on gold can cause the gold to melt or ablate. The alteration of the support using electromagnetic radiation can occur before or after implantation of a support. For example, fenestrations can be created or enlarged in a support after the support has remained in an eye for a period of time to enhance drainage.

While the inventive devices, kits and methods have been described in some detail by way of illustration, such illustration is for purposes of clarity of understanding only. It will be readily apparent to those of ordinary skill in the art in light of the teachings herein that certain changes and modifications may be made thereto without departing from the spirit and scope of the appended claims. For example, it is envisioned that the devices, kits and methods can be applied to nonhuman eyes to reduce intraocular pressure, e.g., in dogs, cats, primates, or horses.

What we claim is:

1. A device for reducing intraocular pressure in an eye having a Schlemm's canal and a trabecular meshwork, comprising: a support implantable circumferentially within Schlemm's canal and configured to maintain the patency of at least a portion thereof, wherein the support comprises an arcuate member, wherein at least a portion of the arcuate member has a radius of curvature smaller than the radius of curvature of Schlemm's canal so that at least a portion of the arcuate member is configured to extend out of Schlemm's canal and into the trabecular meshwork and wherein the support does not substantially interfere with transmural flow across Schlemm's canal, and wherein when the support is disposed within a cylindrical section of the lumen of the canal having an internal wall surface area C, the support contacts less than 30% of C.

2. The device of claim **1** wherein the support comprises an active agent.

3. The device of claim **2** wherein the support is coated or impregnated with the active agent.

4. The device of claim **2** wherein the active agent is dispersed within the support.

5. The device of claim **2** wherein the active agent is selected from the group consisting of prostaglandins, prostaglandin analogs, beta blockers, alpha-2 agonists, calcium channel blockers, carbonic anhydrase inhibitors, growth factors, antimetabolites, chemotherapeutic agents, steroids, antagonists of growth factors, and combinations thereof.

6. The device of claim **2** wherein the active agent is capable of release using electromagnetic radiation.

7. The device of claim **2** wherein release of the active agent is controllable using a time release system.

8. The device of claim **1** wherein the support has at least one fenestration.

9. The device of claim **1** wherein the shape of the support is capable of alteration using electromagnetic radiation.

10. The device of claim **9** wherein the electromagnetic radiation comprises a laser having a wavelength absorbable by at least one localized portion of the support.

11. The device of claim **1** wherein the support has a circumference equal to about half or less than half of the circumference of Schlemm's canal.

12. The device of claim **1** wherein the support has a circumference equal to about a quarter or less than a quarter of the circumference of Schlemm's canal.

13. The device of claim **1** wherein at least a portion of the support is made from a biocompatible polymer.

14. The device of claim **13** wherein the biocompatible polymer is selected from the group consisting of acrylics and silicones.

15. The device of claim **13** wherein the biocompatible polymer comprises a biodegradable polymer.

16. The device of claim **15** wherein the biodegradable polymer is selected from the group consisting of collagen, a collagen derivative, a poly(lactide); a poly(glycolide); a poly (lactide-co-glycolide); a poly(lactic acid); a poly(glycolic acid); a poly(lactic acid-co-glycolic acid); a poly(lactide)/

poly(ethylene glycol) copolymer; a poly(glycolide)/poly (ethylene glycol) copolymer; a poly(lactide-co-glycolide)/ poly(ethylene glycol) copolymer; a poly(lactic acid)/poly (ethylene glycol) copolymer; a poly(glycolic acid)/poly (ethylene glycol) copolymer; a poly(lactic acid-co-glycolic acid)/poly(ethylene glycol) copolymer; a poly(caprolactone); poly(caprolactone)/poly(ethylene glycol) copolymer; a poly(orthoester); a poly(phosphazene); a poly(hydroxybutyrate) or a copolymer including a poly(hydroxybutyrate); a poly(lactide-co-caprolactone); a polycarbonate; a poly(esteramide); a polyanhydride; a poly(dioxanone); a poly(alkylene alkylate); a copolymer of polyethylene glycol and a polyorthoester; a biodegradable polyurethane; a poly(amino acid); a polyetherester; a polyacetal; a polycyanoacrylate; a poly(oxyethylene)/poly(oxypropylene) copolymer; and blends and copolymers thereof.

17. The device of claim **13** wherein at least a portion of the support is made from polymethylmethacrylate.

18. The device of claim **1** wherein the support is capable of visual enhancement using fluorescence or phosphorescence emission.

19. The device of claim **18** wherein the support comprises a chromophore that fluoresces or phosphoresces upon excitation with a light source.

20. The device of claim **18** wherein the emitted fluorescence or phosphorescence is in the wavelength range of about 300 nm to about 800 nm.

21. The device of claim **1** wherein at least a portion of the support is made from a shape memory material.

22. The device of claim **21** wherein the shape memory material comprises a shape memory polymer.

23. The device of claim **21** wherein the shape memory material comprises a shape memory alloy.

24. The device of claim **23** wherein the shape memory alloy comprises a nickel titanium alloy.

25. The device of claim **21** wherein the support has a compressed state prior to and during implantation and an expanded state following implantation.

26. The device of claim **1** wherein at least a portion of the support is made from a hydrogel.

27. The device of claim **1** wherein at least a portion of the support is made from a biocompatible metal.

28. The device of claim **27** wherein the metal is gold.

29. The device of claim **1** wherein the support comprises at least two adjacent beads.

30. The device of claim **29** wherein the at least two adjacent beads are of different sizes.

31. The device of claim **29** wherein the at least two adjacent beads are of different shapes.

32. The device of claim **29** wherein the shapes of the at least two adjacent beads are independently selected from the group consisting of a sphere, a spheroid, an ovoid, a cylinder, a cuboid, a cube, a cone, a discoid, a coil, and combinations and segments thereof.

33. The device of claim **29** further comprising a connector linking the at least two adjacent beads.

34. The device of claim **33** wherein the connector is flexible.

35. The device of claim **33** further comprising at least three adjacent beads, wherein each bead is linked to its adjacent bead by a connector.

36. The device of claim **35** wherein each connector has a different length.

37. The device of claim **33** wherein the connector comprises the same material as the beads.

38. The device of claim **33** wherein the connector comprises a different material than the beads.

39. The device of claim **33** wherein the connector is also a spacer configured to provide a space between adjacent beads.

40. The device of claim **1** wherein the support comprises at least two discs separated by, and connected with, a connector.

41. The device of claim **40** wherein at least one of the discs has at least one fenestration.

42. The device of claim **1** wherein the support is configured to contact a wall of Schlemm's canal at least at two points.

43. The device of claim **42** wherein the support is configured to contact a wall of Schlemm's canal at least at three points.

44. The device of claim **1** wherein the support is solid.

45. The device of claim **1** wherein at least a portion of the support is hollow.

46. The device of claim **1** wherein at least a portion of the support is porous.

47. The device of claim **1** wherein at least a portion of the support is made of a mesh.

48. The device of claim **1** wherein the support comprises one or more rod-like members.

49. The device of claim **1** wherein the support is capable of being attached to tissue.

50. The device of claim **1** wherein the support contacts less than 10% of C.

51. The device of claim **1** wherein the support contacts less than 1% of C.

52. The device of claim **1** wherein the support is flexible.

53. The device of claim **1** wherein the support is rigid.

54. The device of claim **1** wherein the support has a cross-sectional diameter of about 50 microns to about 500 microns.

55. The device of claim **1** wherein the support has a cross-sectional diameter of about 190 microns to about 370 microns.

56. The device of claim **1** wherein the support does not substantially interfere with longitudinal flow along Schlemm's canal.

57. The device of claim **1** wherein the support does not substantially interfere with transmural flow into and out of Schlemm's canal.

58. A kit for reducing intraocular pressure in an eye having a Schlemm's canal and a trabecular meshwork comprising:

a support implantable circumferentially within Schlemm's canal and configured to maintain the patency of at least a portion thereof, wherein the support comprises an arcuate member, wherein at least a portion of the arcuate member has a radius of curvature smaller than the radius of curvature of curvature of Schlemm's canal so that at least a portion of the arcuate member is configured to extend out of Schlemm's canal and into the trabecular meshwork and wherein the support does not substantially interfere with transmural flow across Schlemm's canal, and wherein when the support is disposed within a cylindrical section of the lumen of the canal having an internal wall surface area C, the support contacts less than 30% of C; and

an introducer for delivering the support.

59. The kit of claim **58** further comprising instructions on using the kit.

60. The kit of claim **58** further comprising an active agent.

61. The kit of claim **58** comprising at least two supports.

62. The kit of claim **61** comprising at least two introducers for delivering the at least two supports.

63. The kit of claim **61** wherein the at least two supports are of different shapes.

64. The kit of claim **61** wherein the at least two supports are of different sizes.

65. The kit of claim **61** wherein the at least two supports comprise different materials.

66. The kit of claim **61** wherein the at least two supports are connected together.

67. The kit of claim **58** further comprising a fixation device for attaching the support to tissue.

68. The kit of claim **58** further comprising a system for visually enhancing the support.

69. The kit of claim **58** further comprising a positioning device for positioning the support.

70. The kit of claim **58** wherein the support is preloaded into the introducer.

71. The kit of claim **58** wherein the introducer comprises a pusher.

* * * * *

EXHIBIT 3

US009486361B2

(12) **United States Patent**
Badawi et al.

(10) **Patent No.: US 9,486,361 B2**
(45) **Date of Patent: Nov. 8, 2016**

(54) **INTRAOCULAR IMPLANTS AND METHODS AND KITS THEREFOR**

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(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 577 days.

(21) Appl. No.: **13/445,816**

(22) Filed: **Apr. 12, 2012**

(65) **Prior Publication Data**

US 2012/0197176 A1 Aug. 2, 2012

Related U.S. Application Data

(63) Continuation of application No. 12/695,053, filed on Jan. 27, 2010, now Pat. No. 8,287,482, which is a continuation of application No. 11/475,523, filed on Jun. 26, 2006, now Pat. No. 7,909,789.

(51) **Int. Cl.**
A61B 19/00 (2006.01)
A61F 9/007 (2006.01)

(52) **U.S. Cl.**
CPC ***A61F 9/00781*** (2013.01); *A61F 2210/0004* (2013.01); *A61F 2210/0014* (2013.01); *A61F 2250/0067* (2013.01)

(58) **Field of Classification Search**
CPC A61F 9/00781
USPC 604/8, 9, 264; 623/23.64, 23.7
See application file for complete search history.

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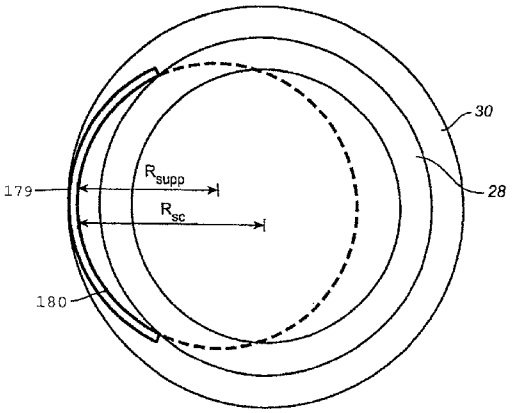
(57) **ABSTRACT**

Devices, methods and kits are described for reducing intraocular pressure. The devices include a support that is implantable within Schlemm's canal and maintains the patency of the canal without substantially interfering with transmural fluid flow across the canal. The devices utilize the natural drainage process of the eye and can be implanted with minimal trauma to the eye. Kits include a support and an introducer for implanting the support within Schlemm's canal. Methods include implanting a support within Schlemm's canal, wherein the support is capable of maintaining the patency of the canal without substantial interference with transmural fluid flow across the canal.

9 Claims, 15 Drawing Sheets



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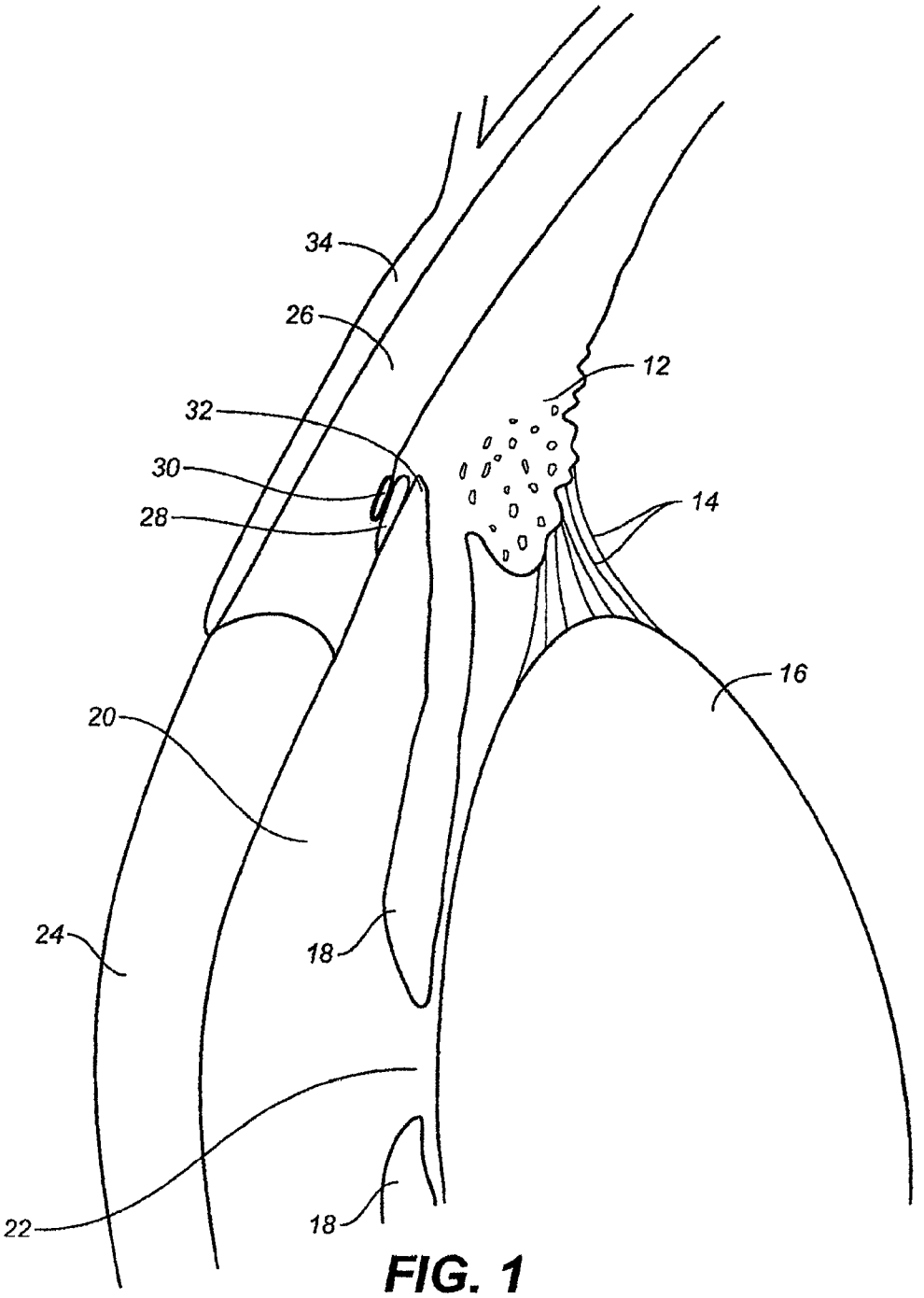


FIG. 1

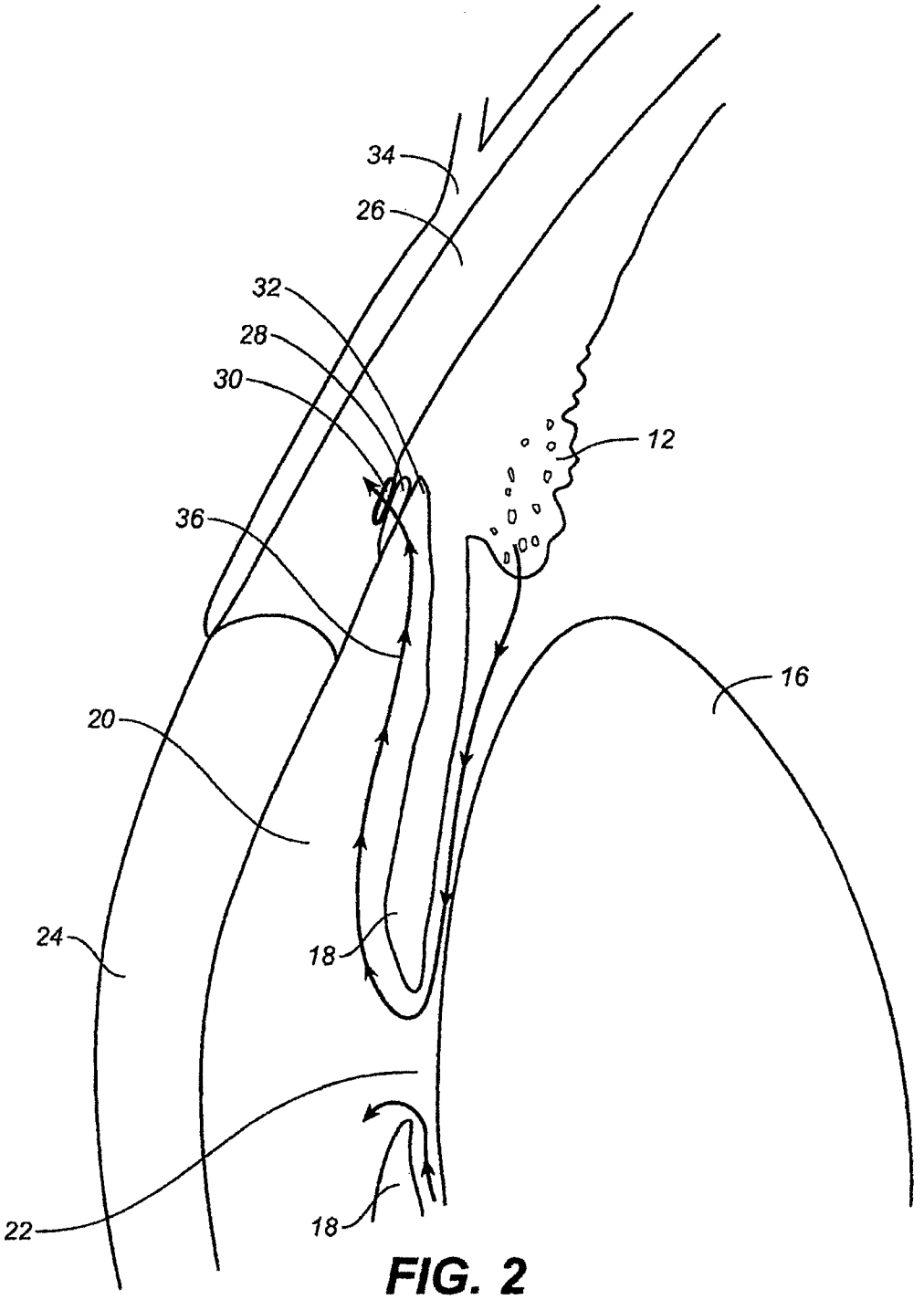


FIG. 2

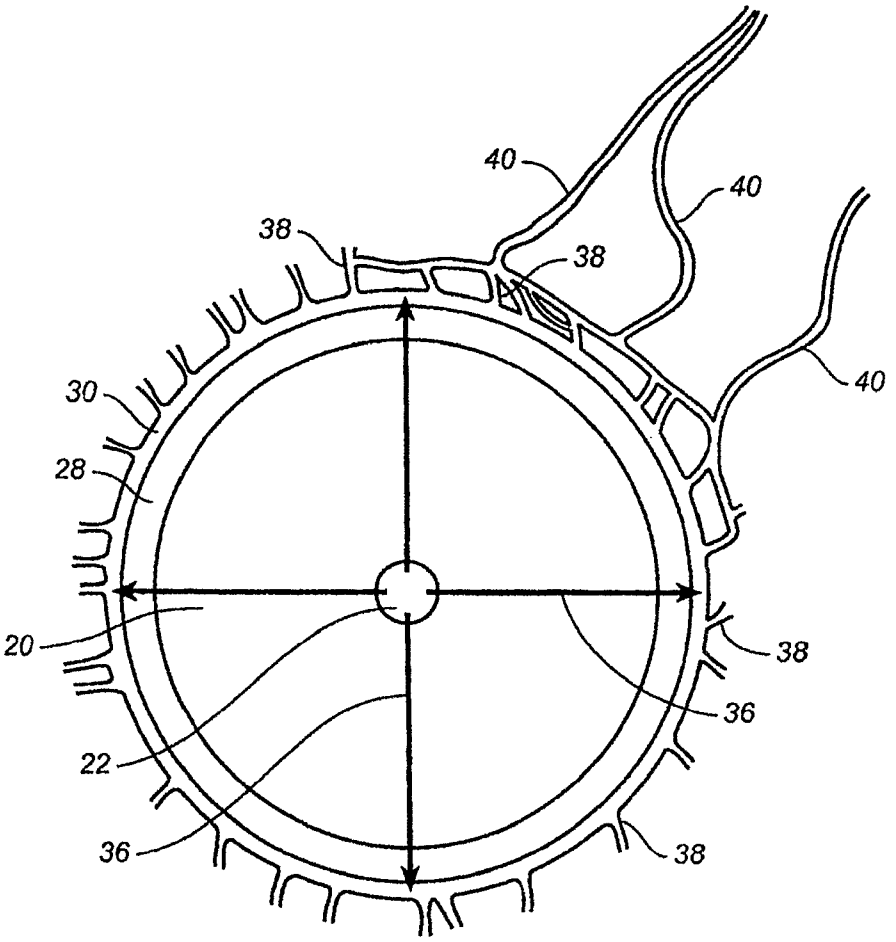


FIG. 3

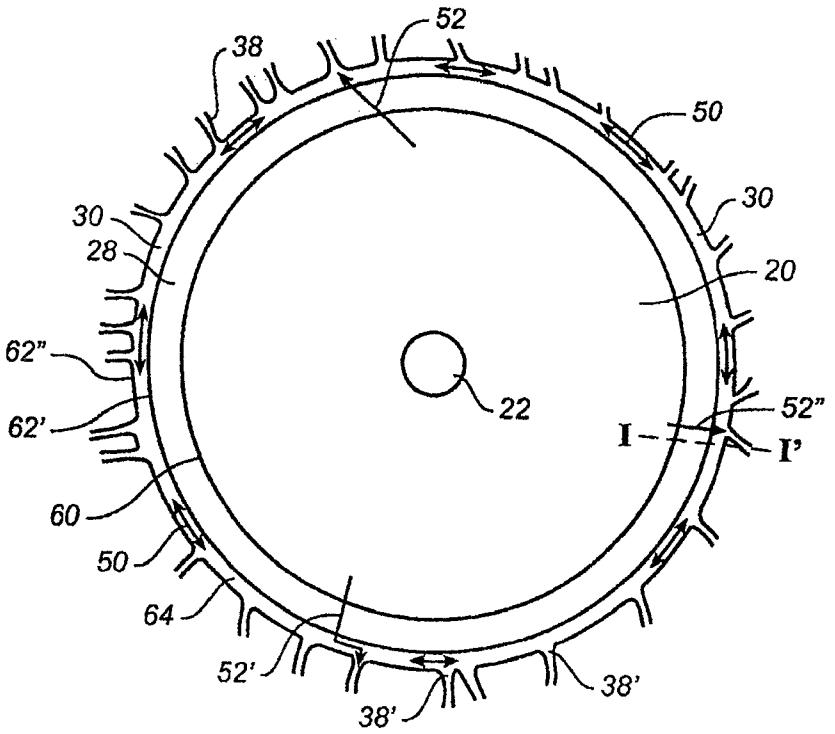
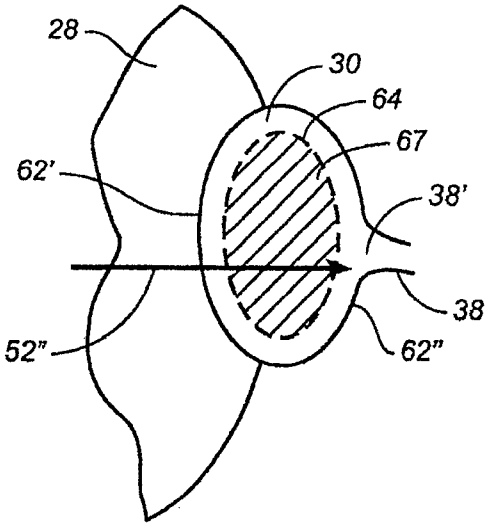

52
38
50
30
30
28
20
62"
22
52"
62'
I
I'
60
50
64
52'
38'
38'

FIG. 4A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30
64
67
62'
38'
38
52"
62"

FIG. 4B

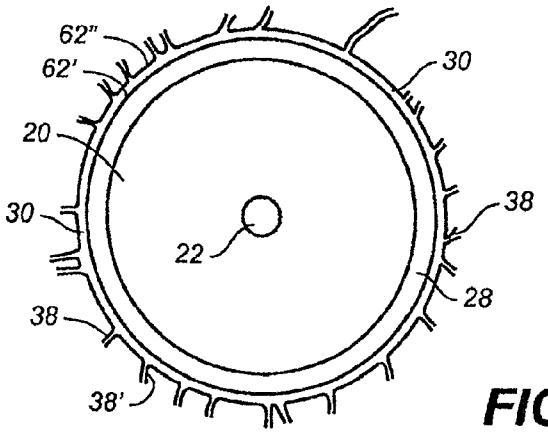

FIG. 5A

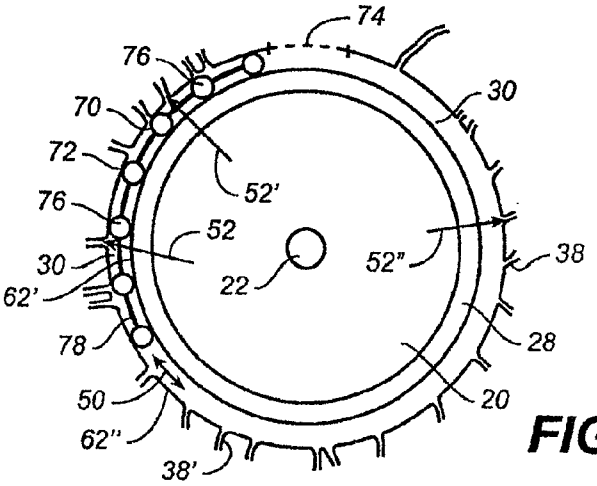

FIG. 5B

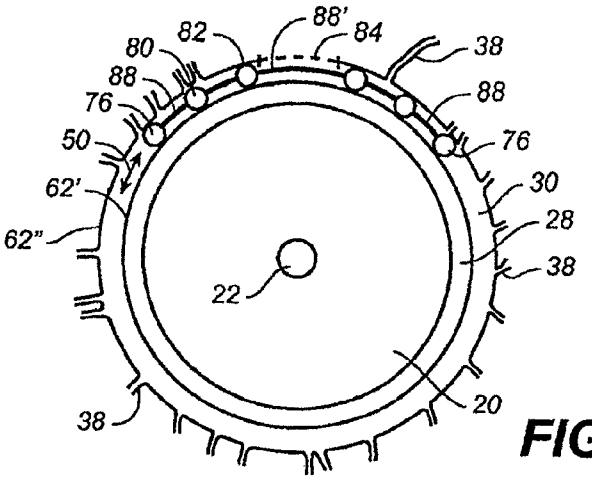

FIG. 5C

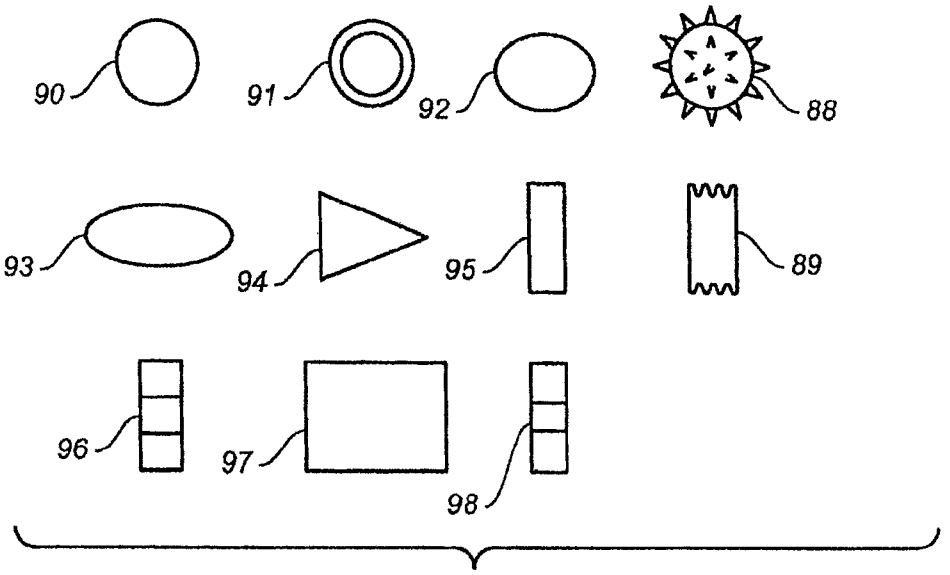

FIG. 6A

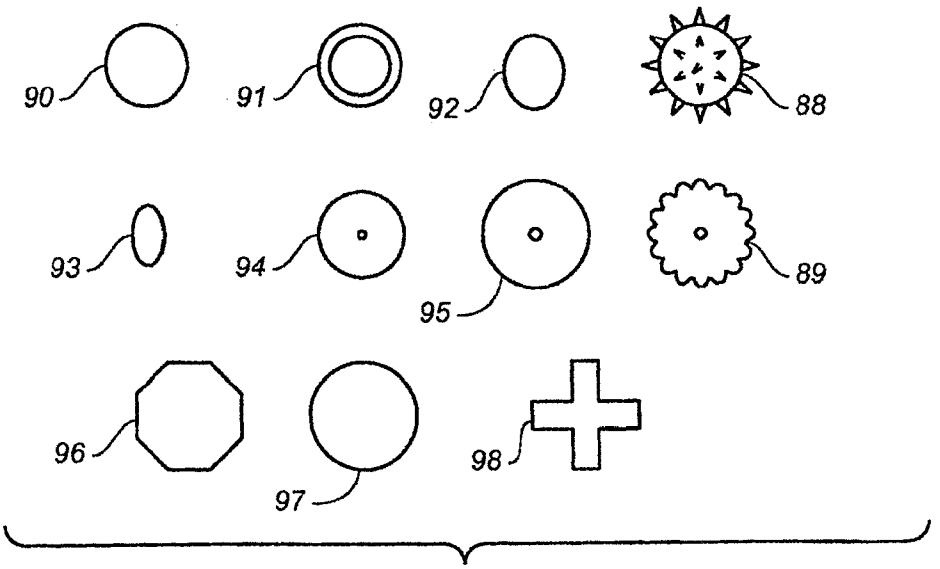

FIG. 6B

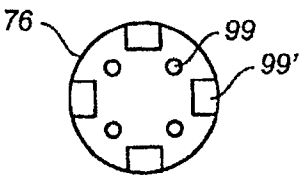

FIG. 6C

FIG. 7A

FIG. 7B

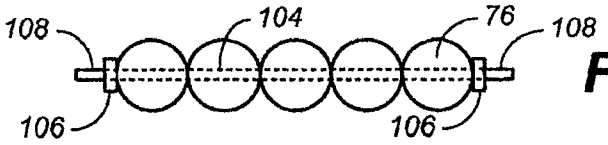

FIG. 7C

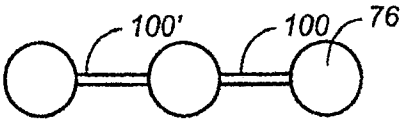

FIG. 7D

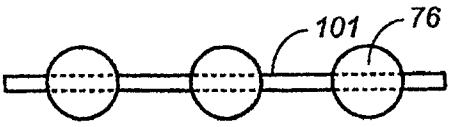

FIG. 7E

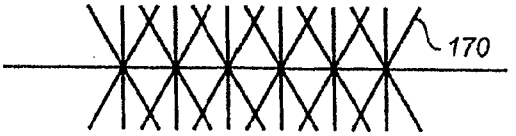

FIG. 8A

FIG. 8B

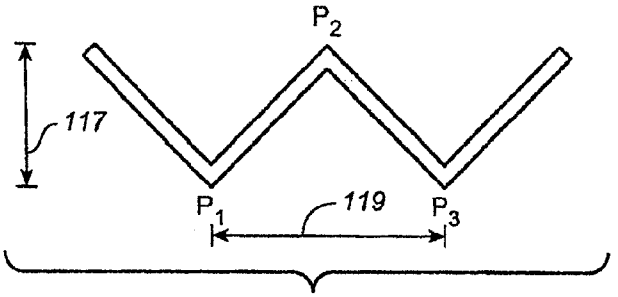

FIG. 8C

FIG. 8D

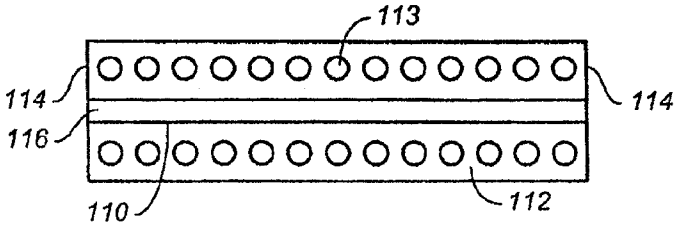

FIG. 8E

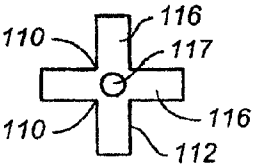

FIG. 8F

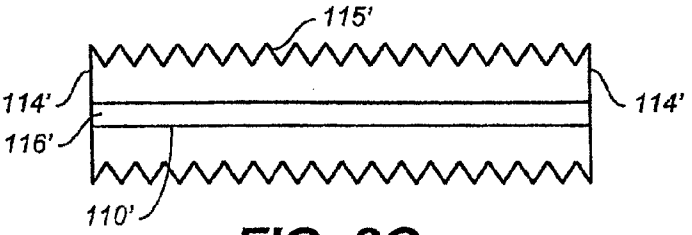

FIG. 8G

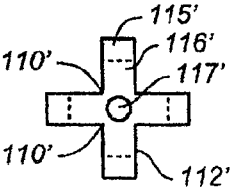

FIG. 8H

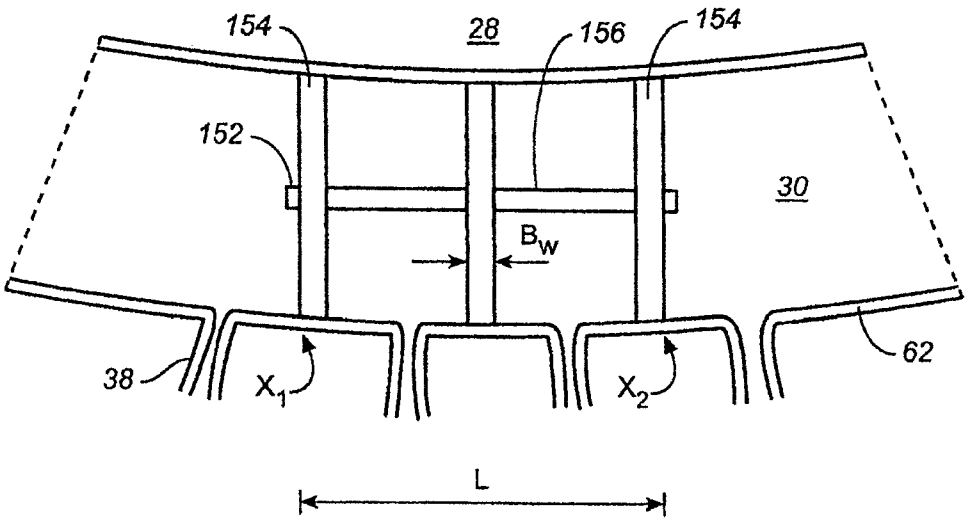
154
28
156
154
152
30
B_W
38
X_1
X_2
62
L

FIG. 9A

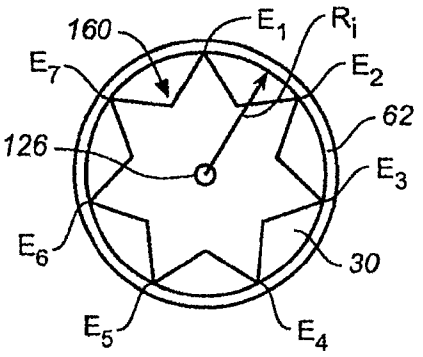
160
E_1
R_i
E_7
E_2
62
126
E_3
E_6
30
E_5
E_4

FIG. 9B

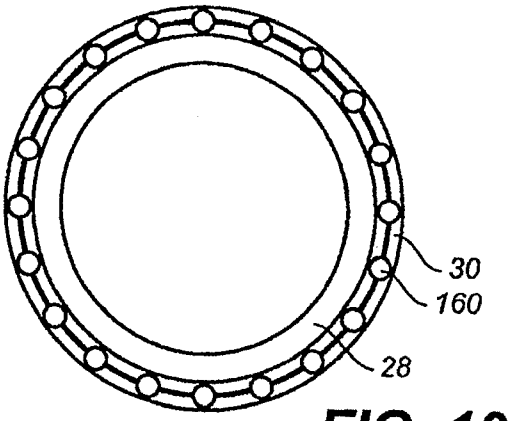

FIG. 10A

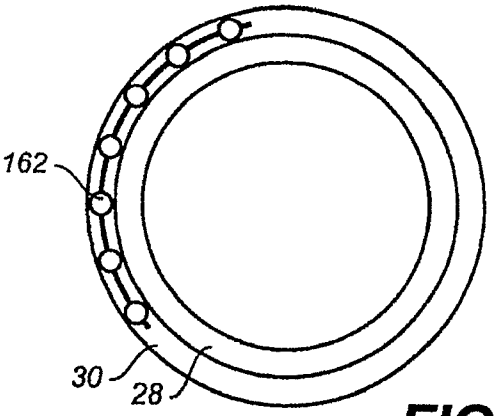

FIG. 10B

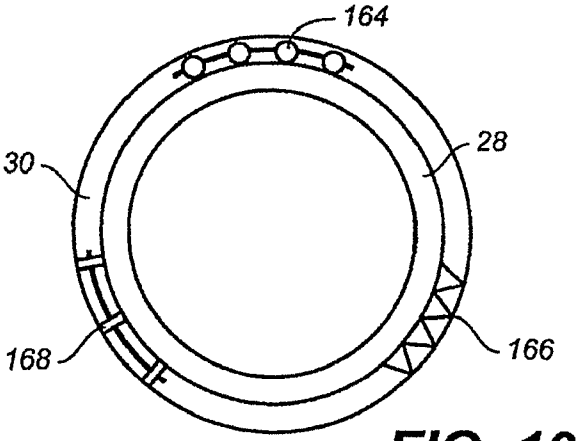

FIG. 10C

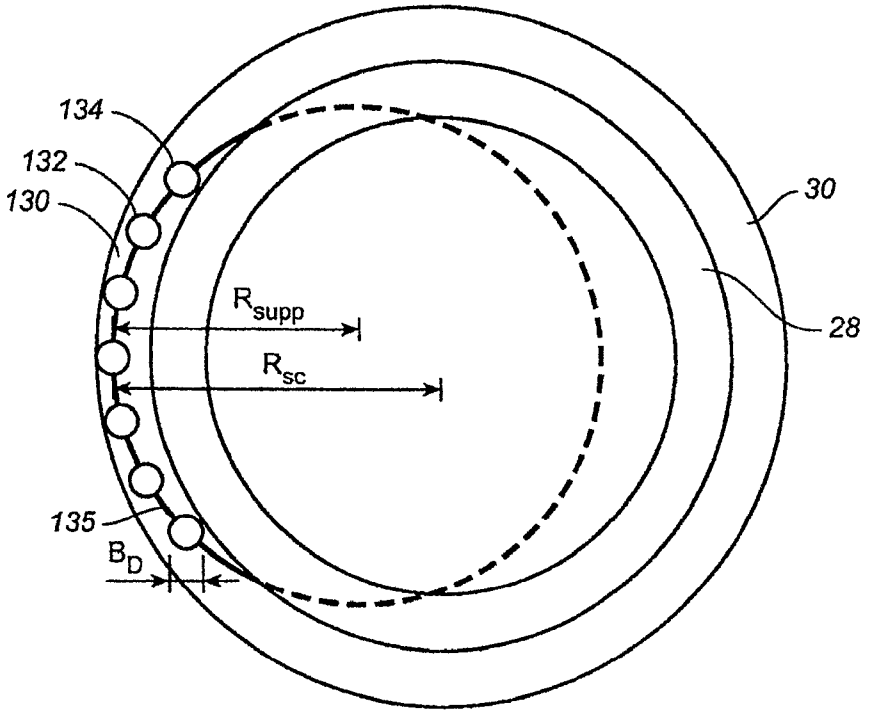

FIG. 11A

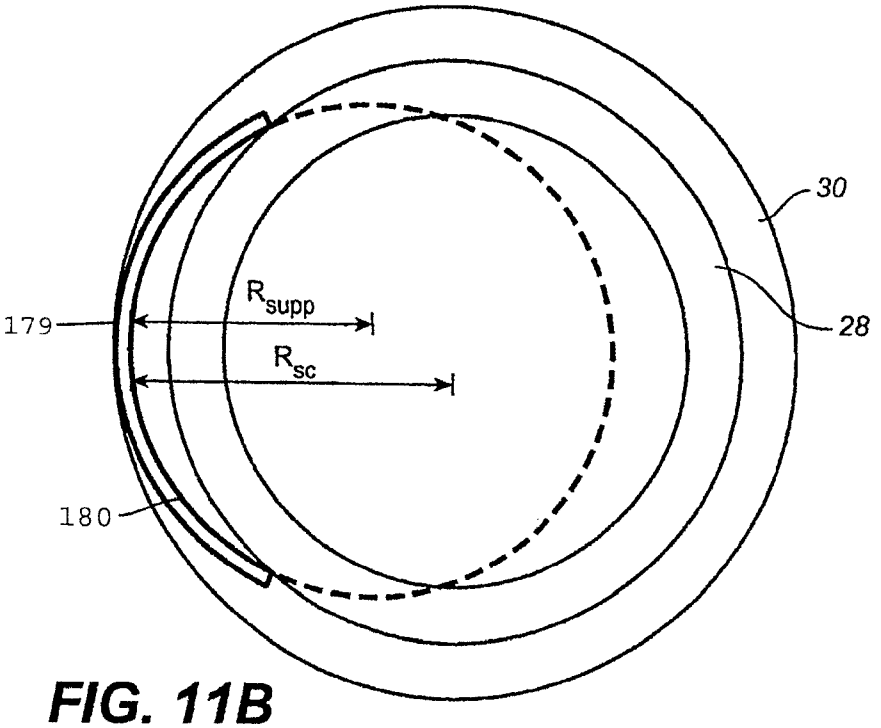

FIG. 11B

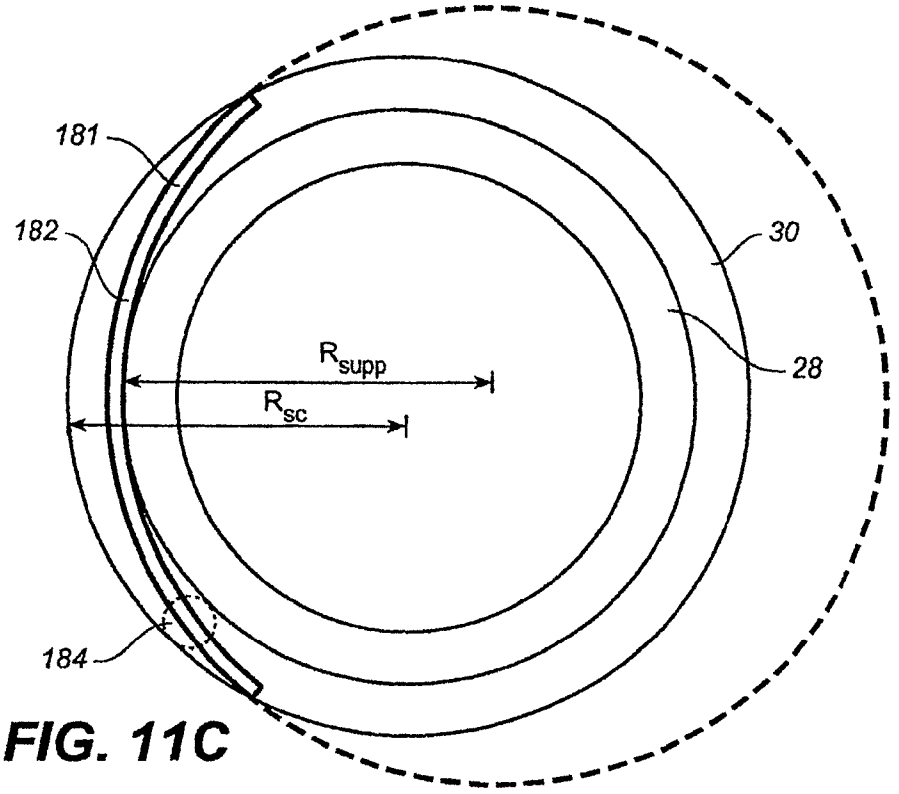

FIG. 11C

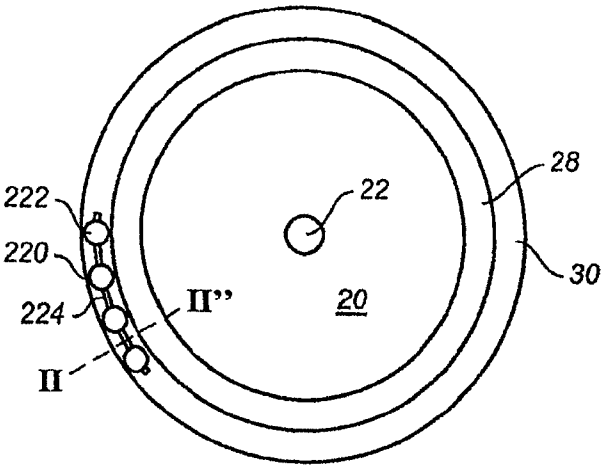

FIG. 12A

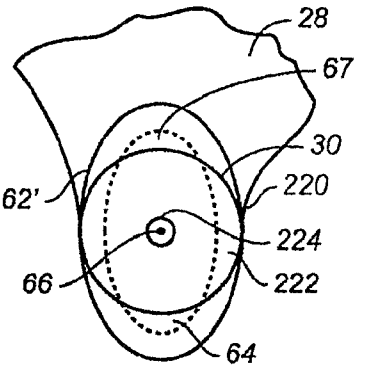

FIG. 12B

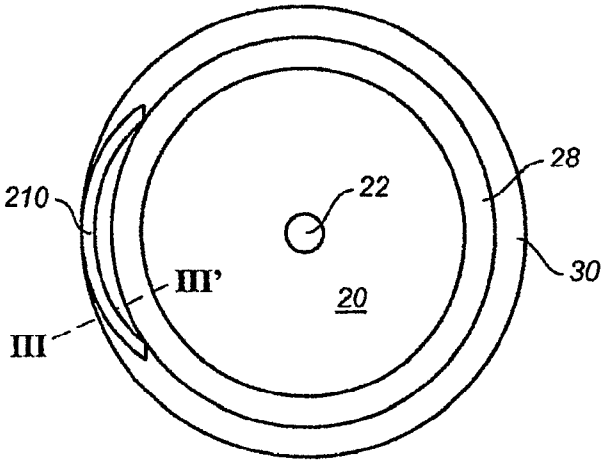

FIG. 12C

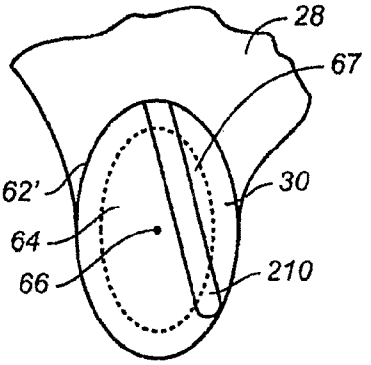

FIG. 12D

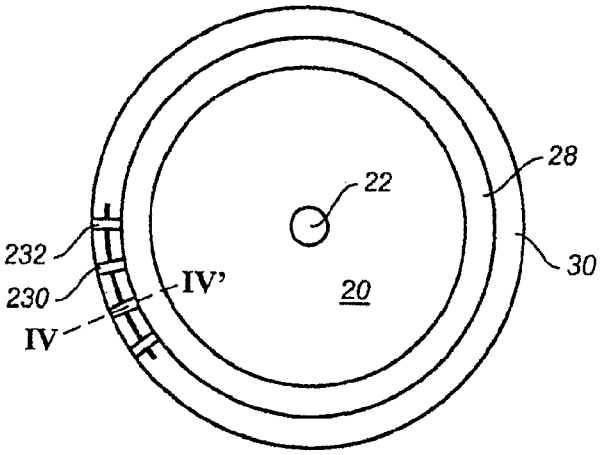

FIG. 12E

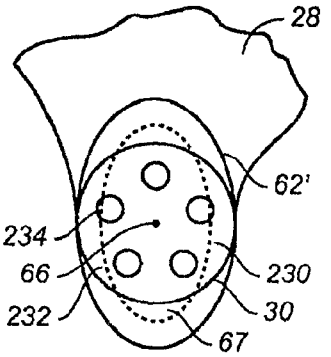

FIG. 12F

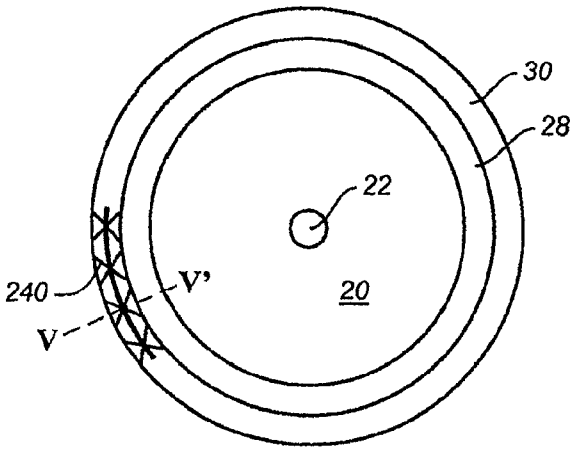

FIG. 12G

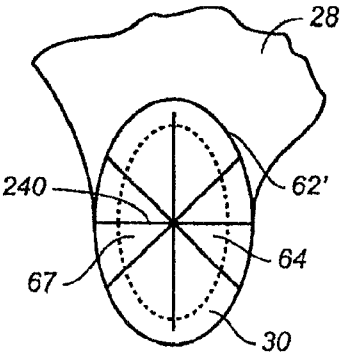

FIG. 12H

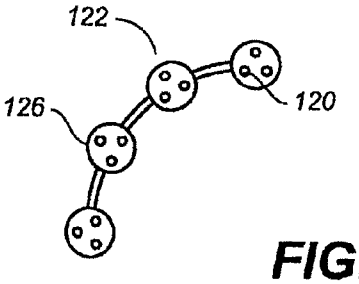

FIG. 13

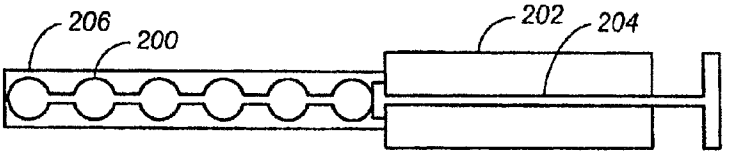

FIG. 14A

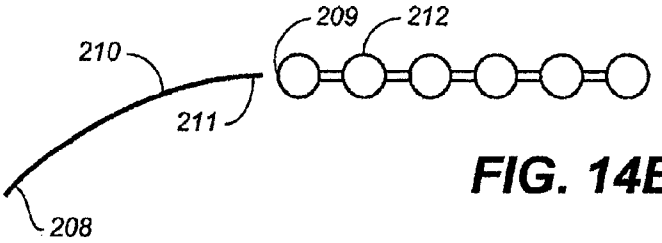

FIG. 14B

FIG. 14C

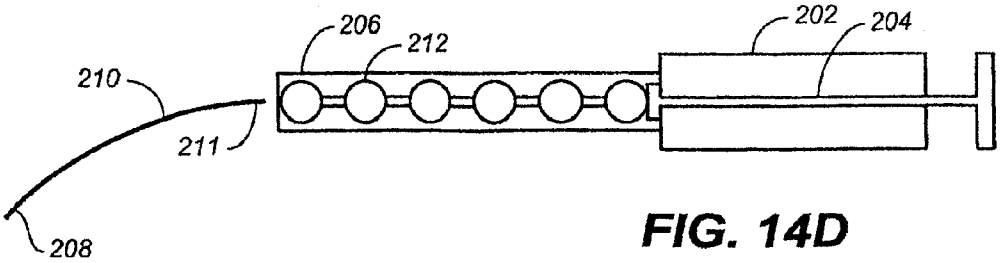

FIG. 14D

INTRAOCULAR IMPLANTS AND METHODS AND KITS THEREFOR

CROSS-REFERENCE TO RELATED APPLICATIONS

This application is a continuation of U.S. patent application Ser. No. 12/695,053, filed Jan. 27, 2010, which is a continuation of U.S. patent application Ser. No. 11/475,523, filed on Jun. 26, 2006 (now U.S. Pat. No. 7,909,789), the disclosures of which are hereby incorporated by reference in their entirety.

FIELD

The devices, kits and methods described herein relate generally to intraocular pressure reduction. More particularly, the devices, kits and methods relate to intraocular implants implantable into Schlemm's canal that can reduce intraocular pressure without substantially interfering with fluid flow across Schlemm's canal.

BACKGROUND

Glaucoma is a potentially blinding disease that affects over 60 million people worldwide, or about 1-2% of the population. Typically, glaucoma is characterized by elevated intraocular pressure. Increased pressure in the eye can cause damage to the optic nerve which can lead to loss of vision if left untreated. Consistent reduction of intraocular pressure can slow down or stop progressive loss of vision associated with glaucoma. In addition, patients are often diagnosed with pre-glaucoma and ocular hypertension when they exhibit symptoms likely to lead to glaucoma, such as somewhat elevated intraocular pressure, but do not yet show indications of optic nerve damage. Treatments for glaucoma, pre-glaucoma and ocular hypertension primarily seek to reduce intraocular pressure.

Increased intraocular pressure is caused by sub-optimal efflux or drainage of fluid (aqueous humor) from the eye. Aqueous humor or fluid is a clear, colorless fluid that is continuously replenished in the eye. Aqueous humor is produced by the ciliary body, and then flows out primarily through the eye's trabecular meshwork. The trabecular meshwork extends circumferentially around the eye at the anterior chamber angle, or drainage angle, which is formed at the intersection between the peripheral iris or iris root, the anterior sclera or scleral spur and the peripheral cornea. The trabecular meshwork feeds outwardly into Schlemm's canal, a narrow circumferential passageway generally surrounding the exterior border of the trabecular meshwork. Positioned around and radially extending from Schlemm's canal are aqueous veins or collector channels that receive drained fluid. The net drainage or efflux of aqueous humor can be reduced as a result of decreased facility of outflow, decreased outflow through the trabecular meshwork and canal of Schlemm drainage apparatus, increased episcleral venous pressure, or possibly, increased production of aqueous humor. Flow out of the eye can be restricted by blockages or constriction in the trabecular meshwork and/or Schlemm's canal.

Glaucoma, pre-glaucoma and ocular hypertension currently can be treated by reducing intraocular pressure using one or more modalities, including medication, incisional surgery, laser surgery, cryosurgery, and other forms of surgery. In the United States, medications or medical therapy are typically the first lines of therapy. If medical therapy is not sufficiently effective, more invasive surgical treatments may be used. In other countries, such as those with socialized medical systems or with nationalized health care systems, surgery may be the first line of therapy if it is considered a more cost effective treatment.

A standard incisional surgical procedure to reduce intraocular pressure is trabeculectomy, or filtration surgery. This procedure involves creating a new drainage site for aqueous humor. Instead of naturally draining through the trabecular meshwork, a new drainage pathway is created by removing a portion of sclera and trabecular meshwork at the drainage angle. This creates an opening or passage between the anterior chamber and the subconjunctival space that is drained by conjunctival blood vessels and lymphatics. The new opening may be covered with sclera and/or conjuctiva to create a new reservoir called a bleb into which aqueous humor can drain. However, trabeculectomy carries both long and short term risks. These risks include blockage of the surgically-created opening through scarring or other mechanisms, hypotony or abnormally low intraocular pressure, expulsive hemorrhage, hyphema, intraocular infection or endophthalmitis, shallow anterior chamber angle, and others. Alternatives to trabeculectomy are actively being sought.

Bypass stents are also used to bridge a blocked trabecular meshwork. Stents can be inserted between the anterior chamber of the eye and Schlemm's canal, bypassing the trabecular meshwork. However, it is difficult to consistently and reliably implant a bypass stent from the anterior chamber into Schlemm's canal. The implant procedure is challenging and stents can become clogged and lose functionality over time. Others have inserted tubular elongated cylindrical hollow stents longitudinally into Schlemm's canal. Cylindrical hollow stents can be configured to allow circumferential fluid flow around the canal. These too can lose functionality over time as a result of occlusion or scarring.

Schlemm's canal is small, approximately 190-370 microns in cross-sectional diameter, and circular. Therefore, it can be difficult or expensive to design and manufacture hollow tubular stents of appropriate dimensions for use in opening Schlemm's canal. In addition, hollow tubular stents can be prone to failure and collapse or occlusion over time, as has been shown for cardiovascular stents. Hollow tubular stents incorporating thin walls are especially prone to failure. Further, the walls of tubular stents placed lengthwise along Schlemm's canal can have significant surface area contact with the trabecular meshwork and/or the collector channels, which can result in blockage of the meshwork or collector channels, substantially interfering with transmural flow across Schlemm's canal and into the eye's collector channels.

Therefore, easily manufacturable, minimally invasive devices for effective, long-term reduction in intraocular pressure are desirable. In addition, methods and kits incorporating such devices are desirable.

SUMMARY

Described here are devices, kits and methods for reducing intraocular pressure. The devices for reducing pressure within the eye comprise a support implantable circumferentially within Schlemm's canal that is configured to maintain the patency of at least a portion of the canal. The support occupies at least a portion of a central core of Schlemm's canal. The support does not substantially interfere with transmural flow across Schlemm's canal, and thereby uti-

lizes the eye's natural drainage pathways. The support can be implanted into Schlemm's canal with minimal trauma to the eye.

The support generally comprises a biocompatible material. At least a portion of the support can be made from a biocompatible polymer, e.g., acrylics, silicones, polymethylmethacrylate, or a hydrogel. In addition, at least part of the support can be made from a biocompatible metal such as gold. In some variations, at least a portion of the support is made from a shape memory material. Suitable shape memory materials include shape memory polymers or shape memory alloys, such as nickel titanium alloys. If a shape memory material is used, the support can have a compressed state prior to and during implantation into Schlemm's canal, and an expanded state following implantation to open the canal.

In some variations, the support is at least partially made from a biocompatible, biodegradable polymer. The biodegradable polymer can be collagen, a collagen derivative, a poly(lactide); a poly(glycolide); a poly(lactide-co-glycolide); a poly(lactic acid); a poly(glycolic acid); a poly (lactic acid-co-glycolic acid); a poly(lactide)/poly(ethylene glycol) copolymer; a poly(glycolide)/poly(ethylene glycol) copolymer; a poly(lactide-co-glycolide)/poly(ethylene glycol) copolymer; a poly(lactic acid)/poly(ethylene glycol) copolymer; a poly(glycolic acid)/poly(ethylene glycol) copolymer; a poly(lactic acid-co-glycolic acid)/poly(ethylene glycol) copolymer; a poly(caprolactone); a poly(caprolactone)/poly(ethylene glycol) copolymer; a polyorthoester; a poly(phosphazene); a poly(hydroxybutyrate) or a copolymer including a poly(hydroxybutyrate); a poly(lactide-co-caprolactone); a polycarbonate; a poly(esteramide); a polyanhydride; a poly(dioxanone); a poly(alkylene alkylate); a copolymer of polyethylene glycol and a polyorthoester; a biodegradable polyurethane; a poly(amino acid); a polyetherester; a polyacetal; a polycyanoacrylate; a poly (oxyethylene)/poly(oxypropylene) copolymer; and blends and copolymers thereof.

The support can comprise an active agent. For example, a support can be coated or impregnated with an active agent. Alternatively, an active agent can be dispersed within the support, e.g., by filling a cavity within the support. The active agent can include a prostaglandin, a prostaglandin analog, a beta blocker, an alpha-2 agonist, a calcium channel blocker, a carbonic anhydrase inhibitor, a growth factor, an anti-metabolite, a chemotherapeutic agent, a steroid, an antagonist of a growth factor, or combinations thereof. The release of the active agent can be controlled using a time release system, e.g., by embedding or encapsulating the active agent with a time release composition.

In some variations, the support will be solid. In other variations, at least a portion of the support will be hollow or porous. The surface of the support may be smooth, rough, spiked, or fluted. In still other variations, at least part of the support will be made from mesh. The support can include at least one fenestration and one or more rod-like members.

In some variations, the support comprises at least two adjacent beads. Adjacent beads can have the same or different sizes and shapes, and can be made from the same or different materials. The bead shapes can be spherical, spheroid, ovoid, cylindrical, cuboid, cubical, conical, discoid, helical, or segments thereof. In some variations, there is a connector linking at least two adjacent beads together. If there is a connector, it can be rigid or flexible. If there is more than one connector, e.g., two connectors inserted between three beads, the connectors may be of the same or different lengths. The connectors can include the same or different material as the beads they connect. A connector can also function as a spacer configured to provide space between adjacent beads. In some variations, the support comprises at least two discs separated by, and connected with, a connector. The discs may include fenestrations. The connector may also comprise a guide wire over which a fenestrated bead can be threaded into the canal of Schlemm.

The support can extend approximately all the way around Schlemm's canal, if the support has a circumference approximately equal to the circumference of Schlemm's canal. Alternatively, the support can extend only about half way around the circumference of Schlemm's canal, or about a quarter way around the canal. In some variations, the support will extend less than a quarter circumference of Schlemm's canal. The support can be configured to contact the inner surface of the wall of Schlemm's canal at two, three or more points. In some variations, the support can be attached to tissue. The support may comprise a stiff arcuate member having a radius of curvature smaller or larger than that of Schlemm's canal.

In some variations, the support can be altered using electromagnetic radiation. For example, a laser having a wavelength absorbable by at least one localized portion of the support can be used to alter the support. In other variations, electromagnetic radiation can be used to release an active agent from the support. In still other variations, the support can be visually enhanced using fluorescence or phosphorescence emission. For example, the support can comprise a chromophore that fluoresces or phosphoresces upon excitation with a light source. In some variations, the emitted fluorescence or phosphorescence is in the wavelength range of about 300 nm to about 800 nm. In some variations, the support can comprise a chromophore that enhances postoperative monitoring of the support.

Kits for reducing intraocular pressure are also provided. The kits contain a support that can be implanted circumferentially within Schlemm's canal. The support is configured to maintain the patency of at least part of Schlemm's canal. The support occupies at least a portion of a central core of Schlemm's canal and does not substantially interfere with transmural flow across the canal. The kits also contain an introducer for implanting the support within the canal. In some variations, the kits include a positioning device for adjusting the support within the canal. In other variations, kits include instructions. In still other variations, the kits include an active agent. Some kits contain at least two supports. If more than one support is included, the kits can include at least two introducers for delivering the supports. Multiple supports within the same kit can have the same or different shape, size, or composition. Multiple supports within the same kit can be connected together or remain separate. In some variations, kits include a fixation device for attaching a support to tissue. In other variations, kits may include a system for visually enhancing the appearance of the support.

Methods for reducing intraocular pressure are also described. The methods include inserting a support circumferentially within Schlemm's canal. The support is configured to maintain the patency of at least part of the canal. The support occupies at least a portion of a central core of Schlemm's canal, and does not substantially interfere with transmural flow across the canal. In some variations, the methods also include dilating Schlemm's canal prior to insertion of the support. In still other variations, the methods comprise anchoring the support to tissue. The methods can include implanting at least two supports. If more than one support is implanted within a single eye, the multiple

supports can be positioned circumferentially adjacent to each other or circumferentially opposed (i.e., positioned about 180° apart) to each other within Schlemm's canal. Multiple supports within one eye can be connected or remain separate. In some variations of the methods, the support is illuminated with a light source to visually enhance the position of the support. In other variations of the methods, the support can be altered using electromagnetic radiation. For example, a laser absorbed by at least one localized portion of the support can be used to alter the support. The alteration can comprise the creation or enlargement of an aperture in the support. If electromagnetic radiation is used to alter a support, the alteration can occur before implantation or after implantation.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. **1** provides a partial cross-sectional side view of a normal human eye.

FIG. **2** provides a partial cross-sectional side view of a normal drainage path of fluid from the eye.

FIG. **3** shows a front view of normal fluid drainage from the eye.

FIG. **4**A shows an alternative front view of normal fluid drainage paths from the eye. FIG. **4**B shows a cross-sectional view along line I-I'.

FIG. **5**A provides a front view of an eye in which Schlemm's canal is narrowed or collapsed. FIG. **5**B shows a front view of a device including a support inserted into Schlemm's canal that allows transmural flow across the canal. FIG. **5**C illustrates an alternate design for a device inserted into Schlemm's canal that allows transmural flow across the canal.

FIG. **6**A shows side views of various element or bead configurations that can be used in the supports described herein. FIG. **6**B shows the corresponding front views of the element or bead configurations shown in FIG. **6**A. FIG. **6**C illustrates an element or bead having fenestrations.

FIG. **7**A illustrates a support having multiple juxtaposed beads. FIG. **7**B illustrates a support having multiple juxtaposed and connected beads. FIG. **7**C shows an alternate configuration of a support having multiple juxtaposed and connected beads. FIG. **7**D shows a support having multiple, spaced-apart but connected beads. FIG. **7**E illustrates beads threaded onto a connector.

FIGS. **8**A-B show side and front views, respectively, of a support having an open network structure. FIGS. **8**C-D show side and front views, respectively, of a support having a longitudinal zig-zag configuration that will contact the wall of Schlemm's canal at least three points (labeled P_1, P_2, P_3). FIGS. **8**E-F show side and front views, respectively, of a support having a rod-like member with continuously fluted edges and fenestrations. FIGS. **8**G-H show side and front views, respectively, of another variation of a support having a rod-like member with continuously fluted edges.

FIGS. **9**A-B show expanded cross-sectional views of a support implanted within Schlemm's canal.

FIGS. **10**A-C illustrate various configurations of supports implanted into Schlemm's canal.

FIGS. **11**A-B illustrate two configurations of supports having a smaller radius of curvature than Schlemm's canal. FIG. **11**C shows a support having a larger radius of curvature than Schlemm's canal.

FIG. **12**A illustrates a variation of a support traversing the center of the central core of Schlemm's canal. FIG. **12**B shows a cross-sectional view along line II-II'. FIG. **12**C illustrates a variation of a support traversing the central core of the canal. FIG. **12**D shows a cross-sectional view along line III-III'. FIG. **12**E illustrates a variation of a support that occupies the majority of the central core of the canal. FIG. **12**F shows a cross-sectional view along line IV-IV'. FIG. **12**G illustrates a variation of support having an open network that occupies a portion of the central core of the canal. FIG. **12**H shows a cross-sectional view along line V-V'.

FIG. **13** shows an illustrative example of a support that can be modified using electromagnetic radiation.

FIG. **14**A illustrates a syringe that can be used to insert a support into Schlemm's canal. FIG. **14**B illustrates a variation in which a support is threaded onto a guide element for insertion and positioning in Schlemm's canal. FIG. **14**C illustrates a cross-sectional view of a support having a central bore to accommodate a guide element. FIG. **14**D illustrates a variation in which a syringe and a guide element are used for insertion and positioning of a support in Schlemm's canal.

DETAILED DESCRIPTION

Described here are devices, kits and methods to reduce intraocular pressure by maintaining or restoring Schlemm's canal so that at least a portion of the canal is patent or unobstructed. The devices, kits and methods operate to keep Schlemm's canal from collapsing while not substantially interfering with the eye's natural drainage mechanism for aqueous humor, in which transmural fluid flow across Schlemm's canal occurs. The devices are implantable in Schlemm's canal with minimal trauma to the eye.

With reference to the figures, FIG. **1** shows a partial cross-sectional view of the anatomy of a normal human eye. Ciliary body **12** is connected to iris **18** and to lens **16** via zonular fibrils **14**. The anterior chamber of the eye **20** is bounded on its anterior (front) surface by cornea **24**. In the center of iris **18** is pupil **22**. Cornea **24** is connected on its periphery to sclera **26**, which is a tough fibrous tissue forming the white shell of the eye. Trabecular meshwork **28** is located on the outer peripheral surface of anterior chamber **20**. The trabecular meshwork extends 360° circumferentially around the anterior chamber. Located on the outer peripheral surface of meshwork **28** is Schlemm's canal **30**. Schlemm's canal extends 360° circumferentially around the trabecular meshwork. At the apex formed between iris **18**, meshwork **28** and sclera **26** is angle **32**. Conjunctiva **34** is a membrane overlaying sclera **26** and lining the inside of the eyelid (not shown).

FIG. **2** shows a partial cross-sectional view of flow of aqueous humor within and out of a normally functioning human eye. Aqueous humor is produced in ciliary body **12** and its path through and out of the eye is indicated by solid directional line **36**. The aqueous humor flows from ciliary body **12**, between lens **16** and iris **18**, through pupil **22** into anterior chamber **20**, across trabecular meshwork **28**, across Schlemm's canal **30**, into aqueous veins or collector channels (not shown) and finally into the bloodstream via conjunctival vasculature.

FIG. **3** shows a front view of normal flow of aqueous humor out of the eye. Aqueous humor enters anterior chamber **20** via pupil **22**. The fluid flows outwardly toward the periphery of the eye, with the general path of flow indicated by solid directional lines **36**. The fluid crosses trabecular meshwork **28** and traverses Schlemm's canal **30** to reach aqueous veins or collector channels **38**. There are typically 25-30 collector channels located in a human eye. Collector channels **38** are connected to vasculature **40**, whereby the drained aqueous humor enters the bloodstream. Although

the direction of net or bulk fluid flow is depicted as radially outward by directional lines **36** from pupil **22** for simplicity, actual fluid flow in an eye may follow more varied paths.

Different fluid flow paths in and across Schlemm's canal are illustrated in FIGS. **4**A-B. FIG. **4**A shows a front view of an eye, and FIG. **4**B shows an expanded cross-sectional view along line I-I'. Circumferential (i.e., longitudinal) flow along and around circular canal **30** is depicted by directional lines **50**. Fluid that does not traverse canal **30** to reach collector channels **38** may not be effectively drained from the eye. Examples of fluid flow paths that can effectively drain the eye are illustrated by directional lines **52**, **52'**, and **52"**. In each of these paths, fluid enters trabecular meshwork **28** along its inner peripheral surface **60** and exits the meshwork along its outer peripheral surface **62'**. Meshwork outer peripheral surface **62'** provides the inner peripheral surface or wall of Schlemm's canal **30**. Transmural fluid flow across Schlemm's canal involves two instances of transmural flow across walls or boundaries. First, fluid must flow from trabecular meshwork **38** through inner peripheral surface or wall **62'** of Schlemm's canal **30** to reach lumen **64** of the canal. Second, fluid must flow from lumen **64** through canal outer peripheral wall **62"** through apertures **38'** to enter collector channels **38**. Finally, the collector channels **38** feed the drained fluid into vasculature. Lumen **64** of canal **30** includes a central core region **67**. Thus, fluid flow from the eye differs from fluid flow in other vessels in the body where fluid need only flow longitudinally along the vessel, such as blood flowing through a vein.

Devices

Devices to reduce intraocular pressure comprising a support that can be implanted circumferentially in Schlemm's canal to maintain the patency of at least a portion of the canal are described here. The support occupies at least a portion of a central core of Schlemm's canal and does not substantially interfere with transmural flow across the canal. By "maintain the patency" of at least a portion the canal, it is meant that the support operates to keep the canal at least partially unobstructed to transmural flow, such that fluid can 1) exit through the trabecular meshwork; 2) traverse the canal; and 3) drain via the collector channels. To maintain the patency of the canal, it is not necessary that the support leave the canal unobstructed in regard to circumferential flow. By "does not substantially interfere" with transmural flow, it is meant that the support does not significantly block either fluid outflow from the trabecular meshwork or fluid outflow to the collector channels. In many variations, the support allows between about 0.1 and about 5 microliters per minute aqueous outflux from the eye through the trabecular meshwork and collector channels. The "central core of Schlemm's canal" refers to the region around the cross-sectional center of the canal in the interior space of the canal lumen, i.e., not on the periphery of the canal. Therefore, a device that occupies at least a portion of a central core of Schlemm's canal can traverse at least a portion of the canal's lumen.

Therefore, devices described here need not comprise an open-ended tubular support placed longitudinally along Schlemm's canal, i.e., the devices and supports can be non-tubular. A longitudinal, open-ended tubular support can enable longitudinal flow along the canal. However, even if fluid can flow longitudinally (i.e., circumferentially) along Schlemm's canal, the eye may not be effectively drained unless the fluid eventually traverses the canal. That is, transmural fluid flow across two boundaries must occur: 1) fluid must flow from the trabecular meshwork through a canal inner wall coincident with an outer peripheral boundary of the trabecular meshwork to reach the canal lumen; and 2) fluid must flow from the canal lumen through apertures in the canal outer peripheral wall to reach the connector channels. The collector channels are then able to further disperse the fluid and complete the natural draining process. A tubular support inserted longitudinally into the canal can have significant surface area overlap with surfaces of the canal such that transmural flow across the canal may be significantly impeded. A longitudinal tubular support placed in Schlemm's canal may block flow into the canal from the trabecular meshwork and block flow out of the canal into the collector channels.

Devices described herein for treating elevated intraocular pressure include a support that is implanted within Schlemm's canal. In many instances, the device will reduce the intraocular pressure by 1-40 mm Hg, for example by at least 2 mm Hg. In other instances, the device will reduce intraocular pressure by at least 4 mm Hg, or at least 6 mm Hg, or at least 10 or 20 mm Hg. In still other instances, the device will operate to bring the intraocular pressure into the range of about 8 to about 22 mm Hg. The support can be configured in a variety of ways to at least partially prop open Schlemm's canal thereby maintaining its patency without substantially interfering with or impeding transmural fluid flow across Schlemm's canal. In some variations, the support may interfere with or block longitudinal flow along or around the canal. In many instances, the support will be contained entirely within Schlemm's canal. In some variations the support will be implanted within the canal, but may extend partially beyond Schlemm's canal, e.g., into the trabecular meshwork.

In some variations, a support to maintain at least partial patency for Schlemm's canal to enable fluid flow between an inner wall of the canal and an outer wall of the canal can comprise elements or structures such as bead-like elements or beads, which can be connected together, e.g., as a string of beads. Individual elements or beads or a connected group of elements or beads can be inserted directly into Schlemm's canal. A more detailed description of supports incorporating elements or beads is provided below.

FIG. **5**A illustrates a front view of an eye having a narrowed or collapsed Schlemm's canal **30**, where canal outer peripheral wall **62"** is very close to canal inner peripheral wall **62'**. Although Schlemm's canal **30** is depicted in FIG. **5**A as being uniformly narrow around the entire circumference of canal, it is possible that only a portion of Schlemm's canal is narrowed or collapsed. When Schlemm's canal is collapsed or narrowed, net efflux of aqueous from the anterior chamber to the collector channels **38** is diminished, thereby increasing intraocular pressure. As a result, the risk of pre-glaucoma, ocular hypertension, or glaucoma can increase.

FIG. **5**B illustrates an example of a device **70** inserted into Schlemm's canal **30** through incision site **74**. Device **70** in this example is positioned to one side of incision site **74**. Device **70** includes support **72** that is configured to keep Schlemm's canal at least partially open to transmural fluid flow across both canal inner wall **62'** and canal outer wall **62"** to reach collector channels **38** via apertures **38'**. In the example shown in FIG. **5**B, support **72** includes elements or beads **76** connected with connectors **78**. In this variation, the distance between canal inner wall **62'** and outer wall **62"** is approximately determined by the cross-sectional dimension of support **72**, which is in turn determined by the largest cross-sectional diameter of the beads **76**. Therefore, circumferential (i.e., longitudinal) fluid flow around and along the canal **30** indicated by directional line **50** may be inhibited by

the insertion of support **72** into the canal. However, transmural flow across both walls or boundaries of the canal indicated by directional lines **52**, **52'**, **52"** is enhanced by support **72** and fluid is able to reach collector channels **38** and be drained from the eye. As a result, support **72** can effectively reduce intraocular pressure by utilizing the eye's natural drainage mechanism. Incision **74** need only be large enough to accommodate the diameter of beads **76**, so that trauma to the eye is minimized. Beads can have cross-sectional dimensions in the range from about 50 microns to about 500 microns. Insertion of beads having relatively small cross-sectional diameters (e.g., about 50 microns) into Schlemm's canal open the canal less than the normal cross-sectional diameter of the canal, which is about 190 to about 370 microns, but still can maintain the patency of the canal. Insertion of beads having relatively large cross-sectional diameters (e.g., greater than about 300 microns) can open the canal as large as or larger than the canal's normal cross-sectional diameter and also can operate to stretch the trabecular meshwork. Stretching the trabecular meshwork may further enhance drainage.

FIG. **5**C illustrates an alternate configuration of a device **80** inserted into Schlemm's canal **30** through incision site **84**. Device **80** includes support **82** that extends to both sides of incision site **84**. Support **82** includes elements or beads **76** connected with connectors **88** and **88'**. In this example, connector **88'** is of a different length than connectors **88**. As in FIG. **5**B, beads **76** may impede circumferential (i.e., longitudinal) fluid flow around and along canal **30** indicated by directional line **50**. However transmural flow across the canal is enhanced by support **82** that maintains patency across the canal and allows fluid to reach collector channels **38**. If the beads are fenestrated or comprise rough, spiked, or fluted perimeters, then circumferential fluid flow through or around the beads may also occur.

Elements or beads used in a support may be hollow and closed structures, open structures, solid structures, porous structures, or any combination thereof, and may be of any suitable shape. FIGS. **6**A and **6**B illustrate side and front views, respectively, of exemplary elements or beads that may be used in the supports described here. As shown, solid **90** or hollow **91**, spherical **90**, spheroid **92**, ovoid **93**, conical **94**, disk-shaped **95**, polyhedral **96**, rod-like **97**, or beads with fluted edges **98**, rough edges, **89**, or spiked edges **88** may be used. In some instances, it may be desired to round corners or edges of the beads. As illustrated in FIG. **6**C, elements or beads **76** may include fenestrations **99**, **99'**. Fenestrations may have any suitable cross-sectional shape, such as round or quadrilateral. Although a disc-shaped bead **76** is shown in FIG. **6**C, any shape of bead can be fenestrated.

As illustrated in the variations shown in FIGS. **7**A-E, two or more beads **76** in a support may be adjacent to each other. Adjacent beads may be juxtaposed (FIG. **7**A), connected and juxtaposed (FIGS. **7**B and **7**C), or connected together with connectors **100**, **100'** to form intervals between beads (FIG. **7**D). In addition, beads may be threaded onto a connector **101** (FIG. **7**E). Multiple beads used in a single support may have the same or different shapes, and may be made of the same or different materials.

Junctions **102** between beads as shown in FIG. **7**B can be made using any suitable technique, such as by using an adhesive, chemical bonding, mechanical interlocking, or welding. Beads may also be juxtaposed and connected as shown in FIG. **7**C by threading onto a guide element **104**. Guide element **104** can comprise a fiber, a suture, a guide wire, a fixture, or the like. The beads can be fixed in a juxtaposed configuration on a guide element, e.g., by knotting ends of the fiber or by providing other end-blocking devices **106**, such as clips, caps, protrusions, or the like on ends **108** of element **104**. Any or all of the beads can be attached to guide element **104**, e.g., beads occupying end positions may be attached to element **104** and function as blocking beads to keep beads from sliding off ends **108** of element **104**. Alternatively, beads may slide along element **104**. Guide element **104** can be flexible, such as thin polymer threads, such as a suture, or metal wires. Alternatively, element **104** can be flexible but fixable, such as one or more shapeable metal wires that can be bent into a desired position and maintain that position against some amount of external stress or pressure. In other variations, guide element **104** can be rigid, e.g., a molded polymeric piece or a stiff metal piece.

As shown in FIG. **7**D, multiple connectors **100**, **100'** may be used in a single support, with at least one connector inserted between adjacent beads **76**. If multiple connectors are used, they may be of the same or different lengths. In addition, multiple connectors within the same support may be made of the same or different materials, and the connectors may be made of the same or different materials than the beads. Discrete connectors **100**, **100'** can be inserted between beads **76** and attached to adjacent beads using any suitable method including using adhesives, chemical bonding, welding, mechanical interlocking, knots, or any combination thereof. In some variations, connectors **100**, **100'** between beads can be configured to function as spacers between individual beads. As illustrated in FIG. **7**E, beads **76** can also be threaded onto a connector **101**. If the beads are threaded onto a connector, the beads can be maintained in fixed positions along the connector **101** by any suitable method, including using adhesives, chemical bonding, welding, clips, protrusions on the connector, mechanical interlocking locking between a connector and a bead, knots, or any combination thereof. Alternatively, some or all beads may slide along connector **101**. Connectors **100**, **100'**, **101** can be flexible, such as thin polymer threads or metal wires. Connectors **100**, **100'**, **101** can also be flexible but fixable, such as shapeable metal wires. Alternatively, connectors **100**, **100'**, **101** may be rigid, such as molded polymeric connectors or stiff metal connectors.

Supports of the devices described here need not contain beads. For example, a support can be a unitary structure of fixed or variable length. Supports can be solid, hollow, or porous, or any combination thereof. For example, a support can be partially solid and partially hollow. Examples of support configurations are shown in side view and front view in FIGS. **8**A-F. As illustrated in FIG. **8**A-B, a support can have an open network structure. Such a support can be fabricated out of shapeable metal wires, for example. The support illustrated in FIGS. **8**A-B will have minimal surface area contact with the walls of Schlemm's canal, i.e., only point contacts at the end of wires or fibers **170**. Alternatively, a support having an open network structure can be at least partially made from a mesh or foam. The mesh or foam can be made of any suitable material, e.g., metal or plastic. As shown in FIGS. **8**C-D, the support can have a sinusoidal or zig-zag configuration extending along a selected length of Schlemm's canal. For the example shown in FIG. **8**C, the support will contact the wall of Schlemm's canal at least three points, labeled P_1, P_2, and P_3, after implantation. In FIGS. **8**E-H, examples of rod-like supports having fluted edges are shown. In FIGS. **8**E-F, fluted edges **110** extend longitudinally along sides **112** between ends **114** of the support to form structures **116**. Structures **116** can include fenestrations **113**. The support can include central bore **117**. In FIGS. **8**G-H, fluted edges **110'** extend along sides **112'** to

form structures **116'**. Structures **116'** have serrated outer surfaces **115'** extending between ends **114'**. The support can include central bore **117'**. In the variations illustrated in FIGS. **8**E-H, the support may contact the canal walls at least four points. In some variations, the support is adjustable.

A common characteristic of the support configurations described here is that they need not have continuous or extensive contact with a wall of Schlemm's canal. Indeed, many of the described devices and structures have minimal tangential, periodic, or sporadic contact with the wall. The surface of the support can be rough, smooth, spiked or fluted. As the example shown in FIGS. **8**A-B shows, some supports only have point contacts with the canal wall. For the supports shown in FIGS. **5**B-C, the rounded beads of each of the supports make only tangential contact with the canal wall. Bead shapes can be selected or designed to have minimal surface area contact with canal walls, e.g., beads **98** having fluted edges as shown in FIGS. **6**A-B may have low surface area contact with canal walls. In addition, supports having widely spaced apart beads, e.g., by connectors illustrated in FIGS. **7**D-E that can function to space beads at desired intervals to reduce contact with canal walls yet operate to keep the canal open. As illustrated above with respect to FIGS. **8**C-D, in some variations, the support contacts the interior wall of the canal at least two points; or at least three points.

Expanded cross-sectional views of a support **152** implanted circumferentially in Schlemm's canal are provided FIGS. **9**A-B. The fraction of canal wall surface area in contact with a support can be estimated by viewing the inside of Schlemm's canal as a slightly arcuate cylinder C having length L, extending circumferentially from a first end X_1 to a second end X_2 of support **152**, and inside radius R_i. In some variations, the support contacts less than 0.1% or less than 1% of the surface area of the cylinder C as described above. In other variations, the support contacts less than 10% of the surface area of C. In still other variations, the support contacts less than 30% of the surface area of C. For example, the support **152** shown in FIGS. **9**A-B contacts the canal wall **62** only at bead outer peripheral edges at E_1-E_7, along a distance of the bead width B_W. There is no contact with the canal walls where connectors **156** space apart beads **154**, and no contact in fluted regions **160** of beads **154**. The design feature of minimal support contact with canal walls allows a support to maintain patency of the canal without substantially interfering with transmural flow across the canal. If a substantial portion of the surface area of the inner periphery of the canal adjacent to the trabecular network or of the surface area of the outer periphery of the canal where the collector channels are located is blocked, effective fluid flow across the canal may be impaired.

Supports can have variable lengths and thicknesses. For example, the length of supports using beads can be tuned by varying the number, type, or spacing of beads, or any combination thereof. The thickness of a support can be increased by adding one or more beads having larger dimensions. Unitary supports can also be built with varying lengths, or with adjustable (e.g., trimmable) dimensions. For example, for a support made of shapeable metal having a sinusoidal or zig-zag configuration as shown FIGS. **8**C-D, a cross-sectional dimension **117** of the support can be decreased or increased by apply tension along dimension **119**. As illustrated in FIG. **10**A, a support **160** can extend essentially around the entire circumference of Schlemm's canal **30**. Alternatively, a support can extend approximately half way around the circumference of the canal (not shown). As shown in FIG. **10**B, a support **162** can extend less than half way around the canal. As shown in FIG. **10**C, a support **164** can extend a quarter or less of the circumference around the canal. In addition, more than one support **164**, **166**, **168** can be inserted into a single Schlemm's canal. If multiple supports are inserted into a single canal, they can be of different shapes, lengths, materials or sizes.

A support can be configured such that it will open the canal beyond a maximum cross-sectional dimension of the support itself. For example, as illustrated in FIG. **11**A, device **130** comprising support **132** is inserted into Schlemm's canal **30**. Support **132** comprises beads **134** which have a maximum cross-sectional dimension B_D. Support **132** comprises a stiff arcuate element **135** with a radius of curvature R_{supp} smaller than the radius of curvature of Schlemm's canal R_{SC}. The smaller, fixed radius of curvature R_{supp} of arcuate member **135** urges canal **30** to open more than B_D. In another variation shown in FIG. **11**B, support **179** comprises an arcuate member **180** without beads having a radius of curvature R_{supp} that is less than the radius of curvature R_{SC} of the canal. Member **180** is sufficiently stiff to urge the canal open. In another variation shown in FIG. **11**C, support **181** comprises an arcuate member **182** having a radius of curvature R_{supp} larger than that of Schlemm's canal R_{SC}. Member **182** is also sufficiently stiff to urge the canal open. Arcuate members **135**, **180** and **182** can comprise a shape memory material such as Nitinol, for example. As indicated in FIG. **11**C, support **181** can include beads **184**. To urge open the canal, the radius of curvature R_{supp} of an arcuate members can be about 10%, 20%, 30%, 40%, or 50% or smaller or larger than that of Schlemm's canal R_{SC}. For example, an arcuate member can have a radius of curvature of about 3 mm to about 8 mm. In some variations, the radius of curvature of an arcuate member R_{supp} in a support is about 3 mm, or about 4 mm, or about 5 mm. In other variations, the radius of curvature R_{supp} of an arcuate member in a support is about 6 mm, or about 7 mm, or about 8 mm.

The supports described here occupy at least a portion of a central core of Schlemm's canal. The central core of Schlemm's canal is the region around the cross-sectional center of the canal in the interior space of the canal lumen. A support that occupies at least a portion of the central core of the canal can traverse at least a portion of the canal lumen. For example, some variations of supports can traverse the cross-sectional center of the canal at least one point. Referring to FIG. **12**A, a front view of a support **220** having beads **222** connected with connectors **224** is provided. FIG. **12**B shows an expanded cross-sectional view along line II-II'. Support **220** occupies a portion canal central core **67** in canal lumen **64**. Trabecular meshwork **28** is shown adjacent to canal **30**. In this variation, support **220** traverses the cross-sectional center **66** of the canal. In other variations, supports can traverse the lumen of the canal off-center, e.g., appearing as a chord across the canal lumen in cross-section. Referring to FIG. **12**C, a front view of an arcuate support **210** is shown. FIG. **12**D shows an expanded cross-sectional view along line III-III'. Support **210** traverses and occupies a portion of central core **67** in lumen **64** of canal **30** without passing through canal center **66**. In some variations, the support can occupy the majority of the central core of the canal. Referring to FIG. **12**E, a front view of support **230** comprising disc-like beads **232** is shown. A cross-sectional view along line IV-IV' is shown in FIG. **12**F. As illustrated in FIG. **12**F, bead **232** with fenestrations **234** occupies the majority of central core **67** of canal **30**. In other variations, the support occupies only a small portion of the central core of the canal.

For example, in FIG. **12**G, a front view of a support **240** having an open network structure is shown. A cross-sectional view along line V-V' is shown in FIG. **12**H.

A support can made of a variety of different materials. In general, the support should comprise a biocompatible material, such as a biocompatible polymer, ceramic or ceramic composite, glass or glass composite, metal, or combinations of these materials. Examples of biocompatible metals include stainless steel, gold, silver, titanium, tantalum, platinum and alloys thereof, cobalt and chromium alloys, and titanium nickel alloys such as Nitinol. Examples of biocompatible polymers include high density polyethylene, polyurethane, polycarbonate, polypropylene, polymethylmethacrylate, polybutylmethacryate, polyesters, polytetrafluoroethylene, silicone, polyvinyl alcohol, polyvinyl pyrrolidone, polyvinyl chloride, ethyl vinyl acetate, collagen, collagen derivatives, flexible fused silica, polyolefins, NYLON® polymer, polyimide, polyacrylamide, fluorinated elastomers, and copolymers and blends thereof. In addition, biocompatible hydrogels can be used in supports and devices described herein. As discussed in more detail below, biocompatible polymers may be biodegradable. A support can be made of a single material or a combination of materials. In some variations, a support made from a first material is coated with a second material, e.g., to enhance or improve its biocompatibility.

In some examples, the biocompatible polymer in a support will include a biodegradable polymer. Examples of suitable biodegradable polymers include collagen, a collagen derivative, a poly(lactide), a poly(glycolide), a poly (lactide-co-glycolide), a poly(lactic acid), a poly(glycolic acid), a poly(lactic acid-co-glycolic acid), a poly(lactide)/poly(ethylene glycol) copolymer, a poly(glycolide)/poly (ethylene glycol) copolymer, a poly(lactide-co-glycolide)/polyethylene glycol) copolymer, a poly(lactic acid)/poly (ethylene glycol) copolymer, a poly(glycolic acid)/poly (ethylene glycol) copolymer, a poly(lactic acid-co-glycolic acid)/poly(ethylene glycol) copolymer, a poly(caprolactone), a poly(caprolactone)poly(ethylene glycol) copolymer, a polyorthoester, a poly(phosphazene), a poly(hydroxybutyrate) or a copolymer including a poly(hdroxybutyrate), a poly(lactide-co-caprolactone), a polycarbonate, a poly(esteramide), a polyanydride, a poly(dioxanone), a poly(alykylene alkylate), a copolymer of polyethylene glycol and a polyorthoester, a biodegradable polyurethane, a poly(amino acid), a polyetherester, a polyacetal, a polycyanoacrylate, a poly(oxyethylene)/poly(oxypropylene) copolymer, and blends and copolymers thereof.

At least a portion of the support can be made from a shape memory material. For example, shape memory alloys, e.g. a nickel-titanium alloy can be used. In addition, shape memory polymers, e.g., polymers made from copolymerizing monomers oligo(e-caprolactone) dimethacrylate and n-butyl acrylate or polymers based on styrene acrylate, cyanate ester and epoxies, can be used. If a shape memory material is used in the support, the support can have a compressed state prior to and during implantation, and an expanded state following implantation. The use of a compressed state support comprising a shape memory material can allow for a smaller incision and facilitate insertion into a narrowed or compressed Schlemm's canal. Once implanted, the support can be expanding using any suitable method, e.g., thermally activated by body heat or an alternate heat source, to adopt an expanded state, thereby opening the canal.

The support can include an active agent, such as a pharmaceutical. Active agents can include prostaglandins, prostaglandin analogs, beta blockers, alpha-2 agonists, calcium channel blockers, carbonic anhydrase inhibitors, growth factors, such as tissue growth factors and vascular endothelial growth factors, anti-metabolites, chemotherapeutic agents such as mitomycin-C,5-fluorouracil, steroids, antagonists of growth factors such as antagonists of vascular endothelial growth factors, or combinations thereof. The active agent can be provided as a coating on at least a portion of a support. The active agent can be delivered throughout the eye by dissolution or other dispersal mechanisms. Alternatively, at least a portion of the support can be impregnated with the active agent. In other embodiments, the active agent can be dispersed within at least a portion of the support. For example, a cavity in the support can be filled with the active agent.

The delivery of the active agent can be controlled by time-release. For example, the portion of the support containing the active agent can include a time release coating or time release formulation designed to gradually dissipate the active agent over a certain period of time. Biodegradable coatings and formulations for time-release of active agents are known in the art. In some variations, the support can comprise multiple layers, where the layers each comprise an active agent. For example, support layers can be used to release a series of different agents, or a series of doses of the same agent. Such layers can be part of a coating applied to a support, or part of a support body. In addition, the support can comprise biodegradable layers containing no active agent that can be applied or interspersed between other layers to further control delivery of active agents to the eye.

In some variations, it will be desirable to change or alter the support using electromagnetic radiation. For example, at least a portion of a support can be fenestrated, perforated, bent, shaped or formed using a laser to enhance intraocular pressure reduction. As illustrated in FIG. **13**, predetermined localized portions **120** of support **122** can be designed to absorb light of a certain wavelength or wavelength range. Preferential absorption can be achieved by material selection and/or by doping with chromophores. Upon irradiation with sufficient energy at the selected wavelength or wavelength range, the patterned regions **120** will ablate or melt, leaving new or enlarged perforations or indentations in the support. For example, a pulsed titanium sapphire laser operating between about 750 and about 800 nm can be used to ablate gold regions. If beads **126** in support **120** are hollow, then after irradiation and ablation, features **120** will become fenestrations. The fenestrations can be created to make support **122** more porous in nature or to allow release of an active agent from within a support, e.g., from within beads **126**. Alternatively, it is possible to use a mask in combination with electromagnetic radiation to alter a support, such as by patterning or machining. The modification of a support using electromagnetic radiation can be carried out prior to or subsequent to insertion.

In some variations, the visual appearance of the support can be enhanced under certain conditions to facilitate placement or to monitor the position or condition of the support. Visual enhancement can be achieved by incorporating into or onto the support chromophores that fluoresce or phosphoresce upon excitation with a light source. Chromophores can also assist a clinician in verifying the position of the support postoperatively using a gonioscope, for example. Light sources can include lasers, lamps, and light emitting diodes. In some instances, transmission or absorption filters may be used to select the wavelength of the excitation source or to detect or view emission. Emission from a support capable of visual enhancement may be in the wavelength

range of about 300 nm to about 800 nm. The chromophores can be an integral component of the material making up the support, doped into support material, or coated or sprayed onto the support. Visually-enhancing chromophores can be applied on a temporary basis, or on a permanent basis. An example of a suitable chromophore is fluorescein, which can be excited with any laser or lamp emitting at about 400 to about 500 nm. In addition, phosphorus-based chemiluminescent or photoluminescent pigments can be used, which can be selected to absorb at various wavelengths across the visible spectrum.

In some variations, the support may be capable of being attached to tissue. For example, the support may include a hook, loop, clip, extension, or the like that may be easily attached to tissue. The support may also be attached to tissue using sutures or adhesives. The support may be attached to tissue using more than one attachment method, e.g., suturing may be used in combination with a loop, or an adhesive may be used in combination with a hook. In other variations, the support may be allowed to self-position in Schlemm's canal. In still other variations, the support may be mobile within Schlemm's canal.

Kits

Kits for reducing intraocular pressure are provided, where the kits contain at least one support that can be implanted circumferentially within Schlemm's canal configured to maintain the patency of at least a portion of Schlemm's canal. The support occupies at least a portion of a central core of Schlemm's canal and does not substantially interfere with transmural flow across the canal. The kits also provide an introducer or delivery device for implanting the support in the canal. The support and introducer are provided in packaged combination in the kits. The kits can also include instructions for use, e.g., for implanting and inspecting the support.

The introducer can be inserted into the eye and is capable of implanting the support at the desired implantation position within Schlemm's canal. For example, an introducer may include a tubular cannula through which the support may be passed. In addition to a cannula, the introducer may include a tubular or solid pusher rod that can be used to push or advance the support into and/or around Schlemm's canal. Alternatively, a pusher rod or plunger can be used without a cannula to introduce a support into the canal. A support can be installed into the lumen of a cannula prior to insertion, the distal end of the cannula positioned at or near the desired support location, and the pusher rod operated from the proximal end to push the support distally out of the distal end of the cannula and into the canal. The cannula and/or the pusher rod may be flexible and small enough in diameter to extend at least partially around the canal. In some variations, a proximal end of a suture can be introduced into the canal via a cannula and the suture extended circumferentially around the canal. A distal portion of the suture can be connected to the support and force applied to the proximal end of the suture to pull the support into the canal. The support can then be positioned within the canal by pulling the suture in a distal or proximal direction. The suture can be used to anchor the support within the canal. In other variations, the support can be directly introduced into the canal using surgical forceps, or the like.

FIGS. **14**A-D illustrate additional variations for introducing a support into the canal. As shown in FIG. **14**A, a support **200** can be introduced into the canal using syringe **202** and plunger **204**. Syringe **202** has distal end **206** that can be at least partially inserted into or placed adjacent to an opening in the canal. Force in a distal direction is applied to plunger **204**, thereby pushing support **200** into the canal. Referring to FIGS. **14**B-C, distal end **208** of guide element **210** can be at least partially introduced into the canal. Guide element **210** can be a guide wire. Guide element **210** can be extended circumferentially along the canal to aid in positioning the support. Support **212** comprises central bore **218** capable of accommodating guide element **210** such that support **212** can be threaded onto guide element **210** and slidably positioned along the guide element. Once distal end **209** of support **212** is threaded onto guide element **210**, support **212** can be pushed in a distal direction along guide element **210** to insert support **212** into the canal. In some variations, support **212** can remain threaded onto guide element **210**, and guide element **210** can remain in the canal. In other variations, support **212** can be slid off distal end **208** of guide element **210**, and the guide element can be pulled in a proximal direction for removal. Referring to FIGS. **14**C-D, syringe **202** with plunger **204** can be used in combination with a guide element **210**. In this variation, distal end **208** of guide element **210** is inserted at least partially into Schlemm's canal. Guide element **210** can be extended circumferentially along the canal to aid in positioning the support. Support **212** has central bore **218** capable of accommodating guide element **210**. Proximal end **211** of guide element **210** is inserted into bore **218**. Plunger **204** is depressed in a distal direction to push support **212** into the canal and slide support **212** along element **210**. Guide element **210** can remain in the canal or be removed following insertion of the support. Supports **200**, **212** must be sufficiently resilient to withstand force encountered as they are pushed into the canal.

In some variations, a positioning device may be used with the introducer to position or adjust the support within the canal. A positioning device can include a rod, grippers, a clamp, a hook, or the like. In other variations, a device or system capable of dilating the canal to facilitate insertion of a support may be included in the kits, e.g., a syringe or other device capable of injecting fluid into the canal.

In some variations, the kits contain at least two supports. Multiple supports can be implanted within one eye or within multiple eyes. If the kits contain multiple supports, the kits may also contain multiple introducers. Alternatively, the same introducer may be used for implantation of multiple supports, especially if the multiple supports are being delivered to a single eye. If multiple supports are to be delivered with the same introducer, then the multiple supports can be preloaded into the introducer for sterility. If more than one support is included in a kit, the supports may be of different shapes, sizes, lengths, or materials. If the kits contain more than one support to be implanted into a single eye, the supports can be connected together.

The kits can comprise an active agent, such as a pharmaceutical agent. The active agent may be included as an integral part of the support, or may be supplied in kits for application to the support or to the eye during or after implantation. Examples of active agents that may be supplied as part of the kits include prostaglandins, prostaglandin analogs, beta blockers, alpha-2 agonists, calcium channel blockers, carbonic anhydrase inhibitors, growth factors, such as tissue growth factors or vascular endothelial growth factors, anti-metabolites, chemotherapeutic agents such as mitomycin-C,5-fluorouracil, steroids, antagonists of growth factors, such as antagonists of vascular endothelial growth factor, and combinations thereof.

The kits may contain a fixation device for attaching a support to tissue. Such a fixation device can include sutures, hooks, barbs, clips, adhesives, and combinations thereof. In

addition, the kits may include a system for visually enhancing the support to facilitate viewing, positioning, and monitoring of a support. A system for visually enhancing the support can include a light source, a transmission or absorption filter, a mirror, a composition comprising a chromophore capable of fluorescing or phosphorescing that can be applied to the support, or any combination thereof. Chromophores can assist a clinician in verifying the position of the support postoperatively using a gonioscope, for example. The light source is capable of exciting a chromophore contained within or on the support such that the chromophore emits fluorescence or phosphorescence. The emission is preferably within the wavelength range of about 300 nm to about 800 nm. A suitable light source for such a system can comprise a laser, a light emitting diode, or a lamp. In some instances, transmission or absorption filters may be used to further select the wavelength range of the excitation source or view or detect emission from chromophores. One or more mirrors may be used to direct a light source or emitted light, or to view the support.

Methods

Methods for reducing intraocular pressure are also provided. In general, the methods comprise inserting a support circumferentially within Schlemm's canal, such that the support maintains the patency of at least a portion of the canal. The support occupies at least a portion of a central core of Schlemm's canal and does not substantially interfere with transmural flow across Schlemm's canal.

The methods can comprise inserting a support circumferentially into Schlemm's canal using an introducer and/or a positioning device. The introducer can include a cannula and a tubular or hollow pusher rod. The support can be installed in the lumen of the cannula at its distal end and the pusher rod can be inserted into the lumen of the cannula at its proximal end and extended distally to push the support into position in the canal. In some instances, the cannula and/or the pusher rod may be flexible and small enough in diameter to at least partially extend circumferentially around the canal. In some variations of the methods, a positioning device can be used in addition to an introducer. The positioning device can comprise a second rod, a gripper, a hook, a clamp, or the like. In some variations, the methods include illuminating a support with a light source to causes the support to fluoresce or phosphoresce, thus aiding the visual appearance of the support. The illuminating of the support can occur during or after implantation to inspect the support, e.g., to monitor its position, condition, or performance.

In some instances, the methods will also comprise dilating Schlemm's canal prior to insertion of the support. Dilation of the canal can be accomplished by injecting fluid into the canal. For example, a high viscosity fluid such as sodium hyaluronate, or other dilating fluids known in the art, can be used to dilate the canal.

The methods may include implanting more than one support into an eye. In some variations, the methods will include implantation of two or more supports circumferentially adjacent to each other within the canal, and in other variations, the methods will include implantation of supports circumferentially opposed to each other within the canal, e.g., two supports centered about 180° apart around the circumference of Schlemm's canal. Some variations of the methods can comprise connecting together multiple supports in a single eye.

In some variations, the methods can include anchoring the support to tissue surrounding Schlemm's canal. Anchoring the support to tissue can be accomplished in a variety of ways, e.g., by suturing, application of adhesives, installation of hooks, clips, or the like, or combinations thereof. In other variations, the methods can comprise selecting the size of the support such that the support fits securely into the canal by a friction fit. Examples of arcuate supports that can be implanted with a friction fit are illustrated in FIGS. **11**A-C.

The methods described here can also include altering the support using electromagnetic radiation. For example, a support can include regions capable of preferentially absorbing a certain wavelength range. When electromagnetic radiation of the appropriate wavelength range with sufficient energy is incident upon the support, material in the preferentially absorbing regions will melt or ablate, resulting in perforations or indentations in the support at those regions. For example, a pulsed titanium sapphire laser emitting at about 750 nm to about 800 nm incident on gold can cause the gold to melt or ablate. The alteration of the support using electromagnetic radiation can occur before or after implantation of a support. For example, fenestrations can be created or enlarged in a support after the support has remained in an eye for a period of time to enhance drainage.

While the inventive devices, kits and methods have been described in some detail by way of illustration, such illustration is for purposes of clarity of understanding only. It will be readily apparent to those of ordinary skill in the art in light of the teachings herein that certain changes and modifications may be made thereto without departing from the spirit and scope of the appended claims. For example, it is envisioned that the devices, kits and methods can be applied to nonhuman eyes to reduce intraocular pressure, e.g., in dogs, cats, primates, or horses.

What we claim is:

1. A method for reducing intraocular pressure, comprising:

introducing a tubular cannula having a lumen at least partially within Schlemm's canal;

delivering a high viscosity fluid into Schlemm's canal; and

inserting a support into Schlemm's canal by passing the support through the tubular cannula, wherein the support comprises an arcuate member, wherein at least a portion of the arcuate member has a radius of curvature smaller than a radius of curvature of Schlemm's canal, and wherein the support comprises at least one fenestration.

2. The method of claim **1**, wherein the delivered fluid dilates the canal.

3. The method of claim **1**, wherein the high viscosity fluid is sodium hyaluronate.

4. The method of claim **1**, wherein the support is a rigid support.

5. The method of claim **1**, wherein the support contacts the interior wall of the canal at least at three points.

6. The method of claim **1**, wherein the support does not substantially interfere with longitudinal flow along the canal.

7. The method of claim **1**, wherein the support does not substantially interfere with transmural flow across the inner wall of the canal.

8. The method of claim **1**, wherein the support does not substantially interfere with transmural flow across the outer wall of the canal.

9. The method of claim **1**, wherein at least a portion of the support extends out of Schlemm's canal and into the trabecular meshwork.

* * * * *

EXHIBIT 4

US010314742B2

(12) **United States Patent**
Badawi et al.

(10) **Patent No.: US 10,314,742 B2**
(45) **Date of Patent: *Jun. 11, 2019**

(54) **INTRAOCULAR IMPLANTS AND METHODS AND KITS THEREFOR**

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(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 329 days.

This patent is subject to a terminal disclaimer.

(21) Appl. No.: **15/182,165**

(22) Filed: **Jun. 14, 2016**

(65) **Prior Publication Data**

US 2016/0287440 A1 Oct. 6, 2016

Related U.S. Application Data

(60) Continuation of application No. 13/025,112, filed on Feb. 10, 2011, now Pat. No. 9,370,443, which is a (Continued)

(51) **Int. Cl.**
A61F 9/00 (2006.01)
A61F 9/007 (2006.01)

(52) **U.S. Cl.**
CPC ***A61F 9/00781*** (2013.01); ***A61F 9/0017*** (2013.01); *A61F 2210/0004* (2013.01);
(Continued)

(58) **Field of Classification Search**
CPC A61F 9/00781; A61F 2210/0014; A61F 2250/0067
(Continued)

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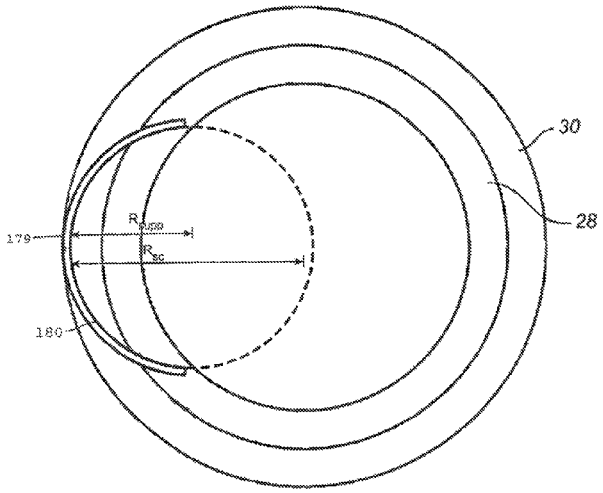
(57) **ABSTRACT**

Devices, methods and kits are described for reducing intraocular pressure. The devices include a support that is implantable within Schlemm's canal and maintains the patency of the canal without substantially interfering with transmural fluid flow across the canal. The devices utilize the natural drainage process of the eye and can be implanted with minimal trauma to the eye. Kits include a support and an introducer for implanting the support within Schlemm's canal. Methods include implanting a support within Schlemm's canal, wherein the support is capable of maintaining the patency of the canal without substantial interference with transmural fluid flow across the canal.

20 Claims, 16 Drawing Sheets



Related U.S. Application Data

division of application No. 11/475,523, filed on Jun. 26, 2006, now Pat. No. 7,909,789.

(52) **U.S. Cl.**
CPC *A61F 2210/0014* (2013.01); *A61F 2250/0067* (2013.01)

(58) **Field of Classification Search**
USPC 604/8, 9, 264; 623/23.64, 23.7
See application file for complete search history.

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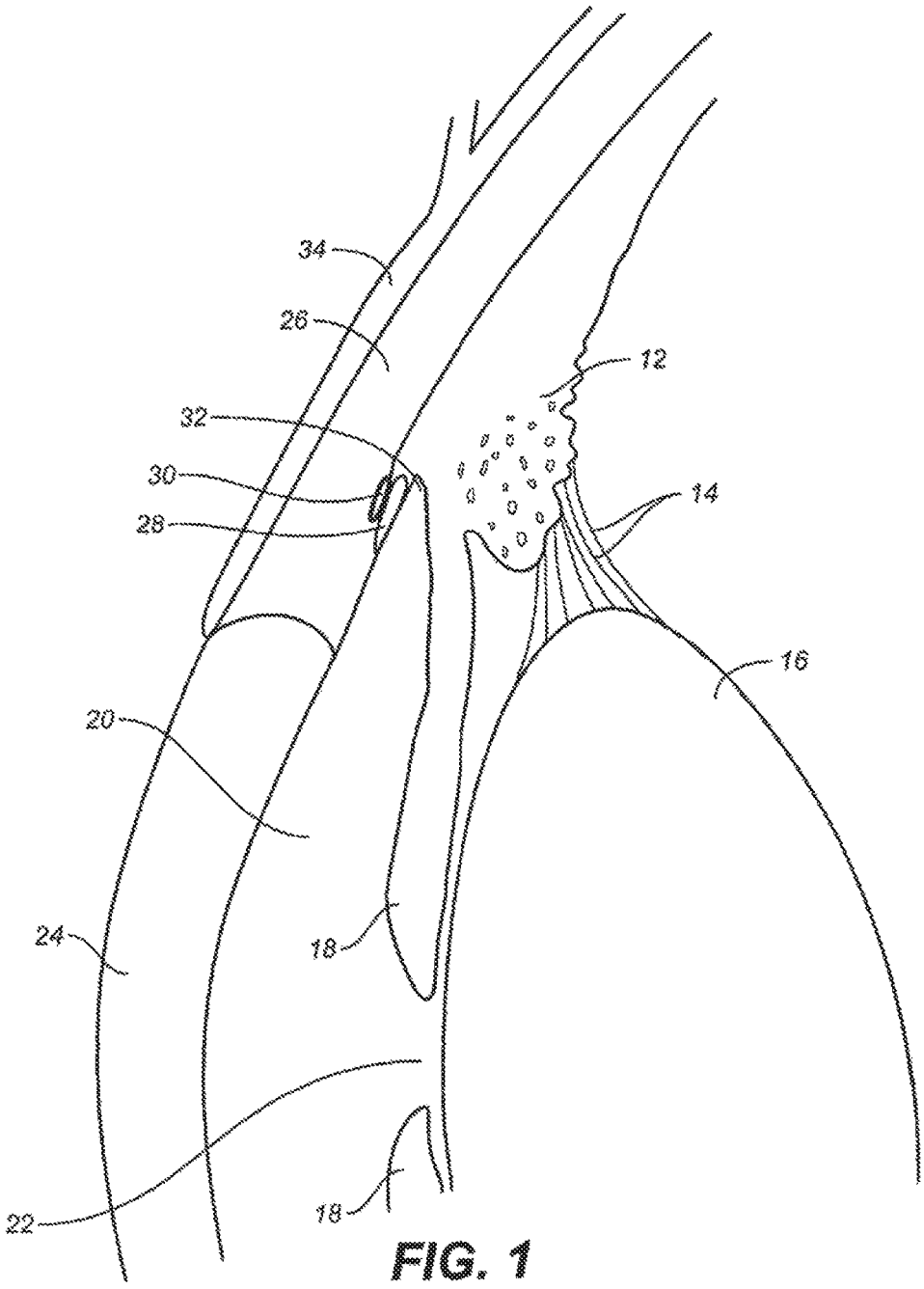


FIG. 1

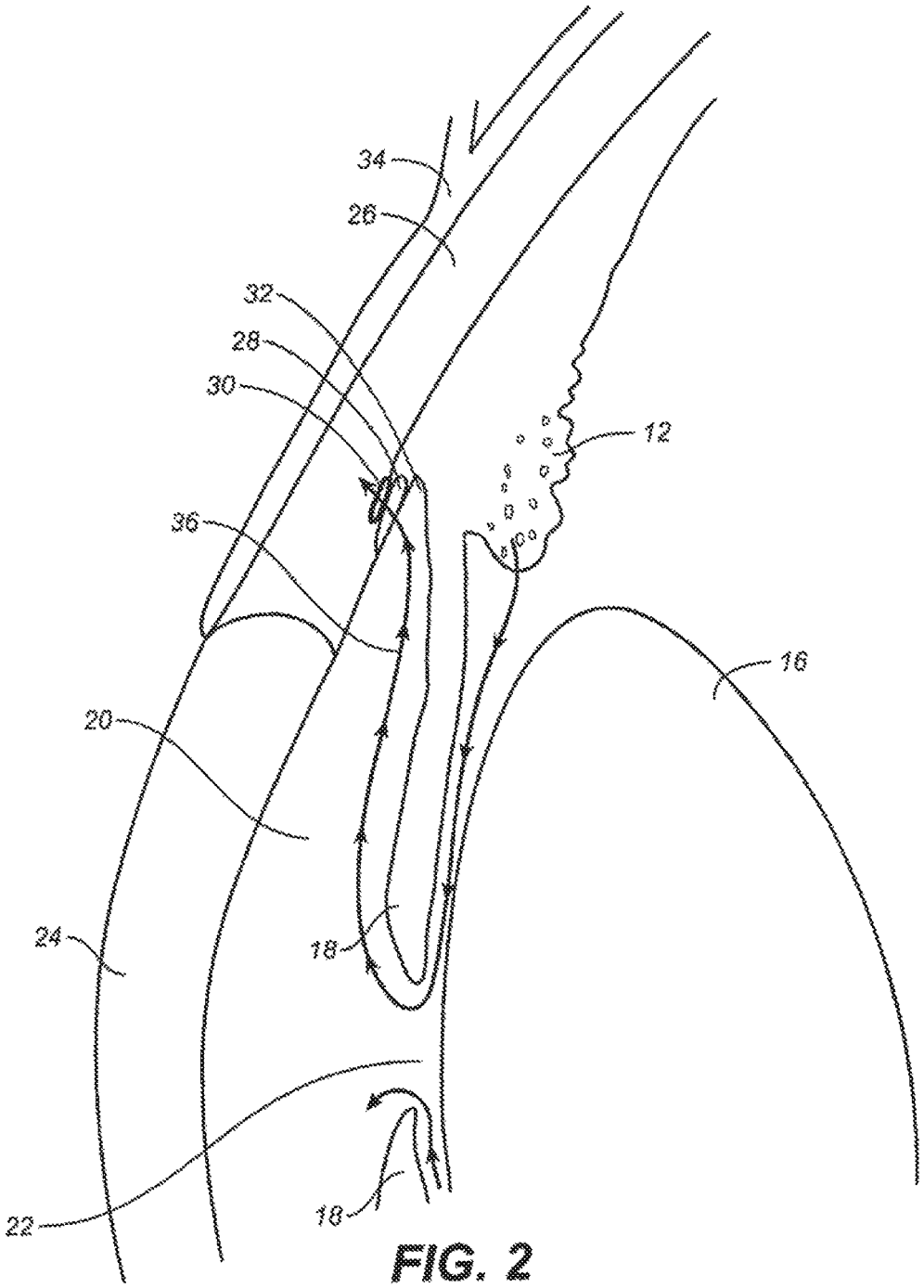


FIG. 2

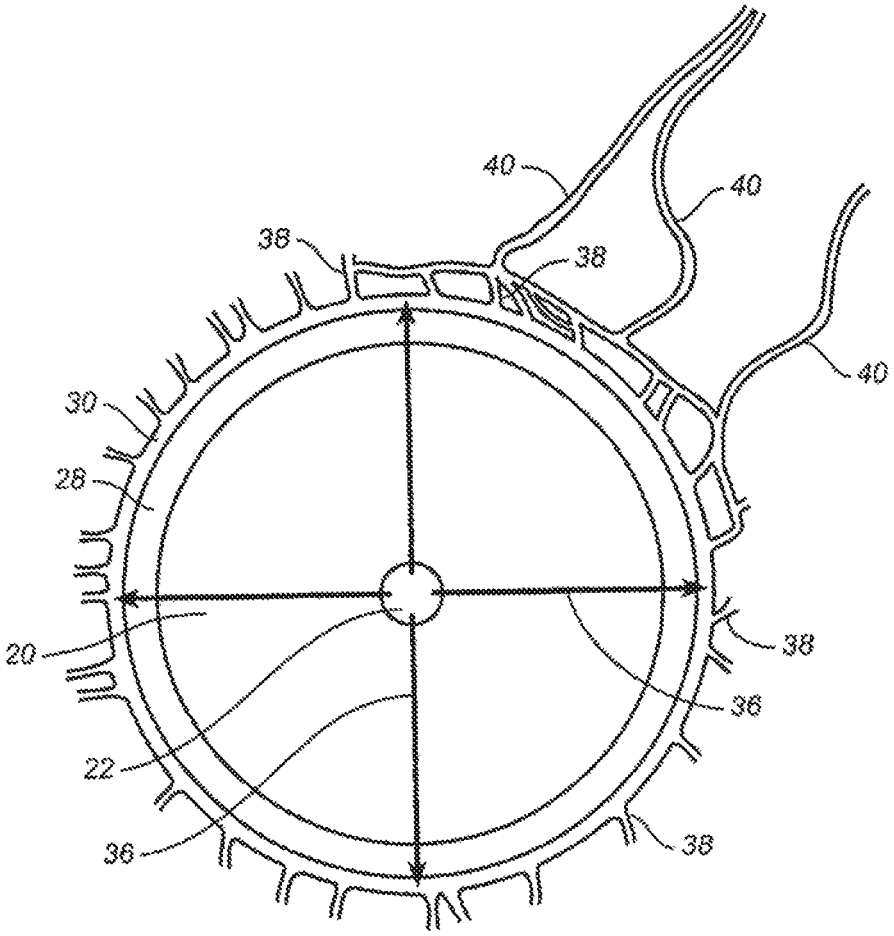
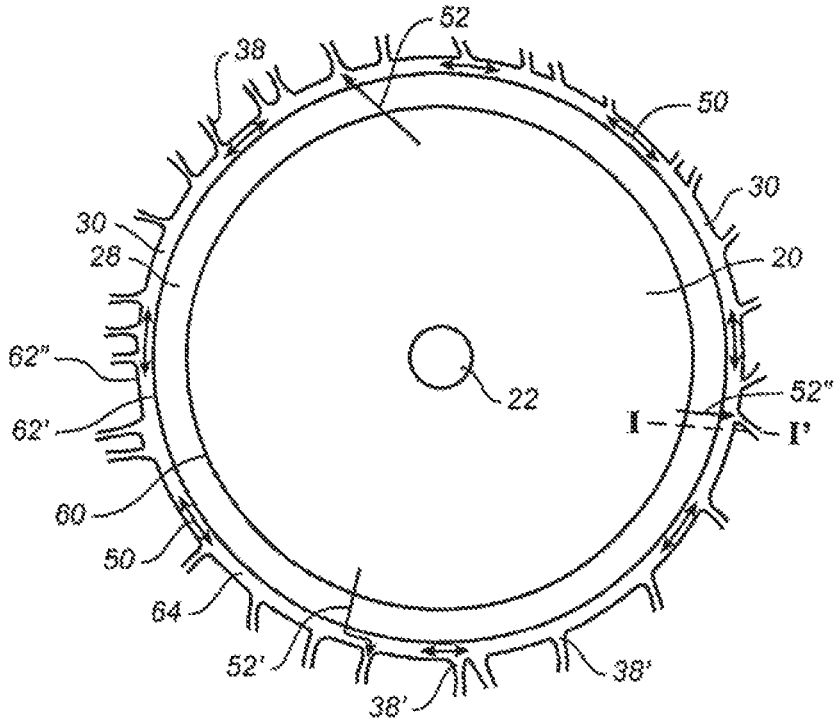


FIG. 3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38'

FIG. 4A

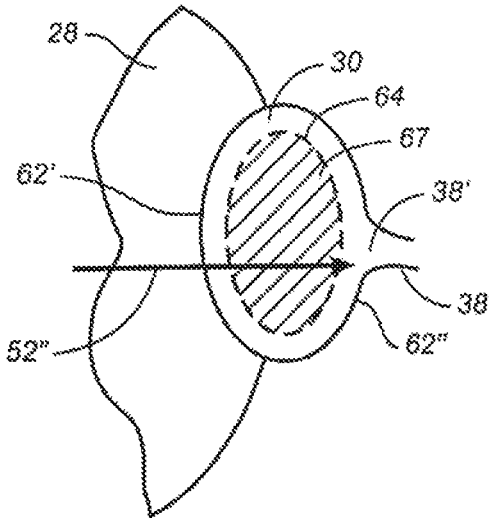
28
30
64
67
62'
38'
38
62"
52"

FIG. 4B

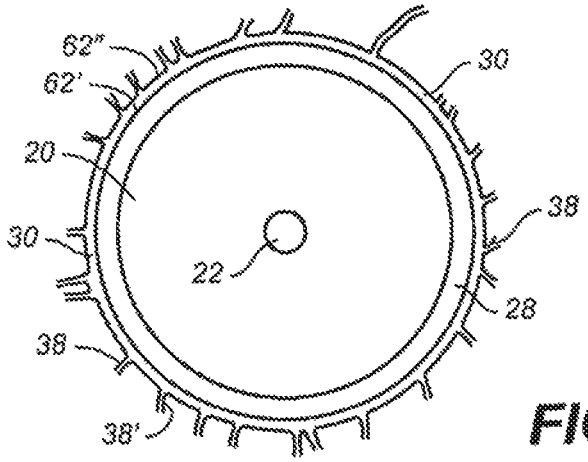

FIG. 5A

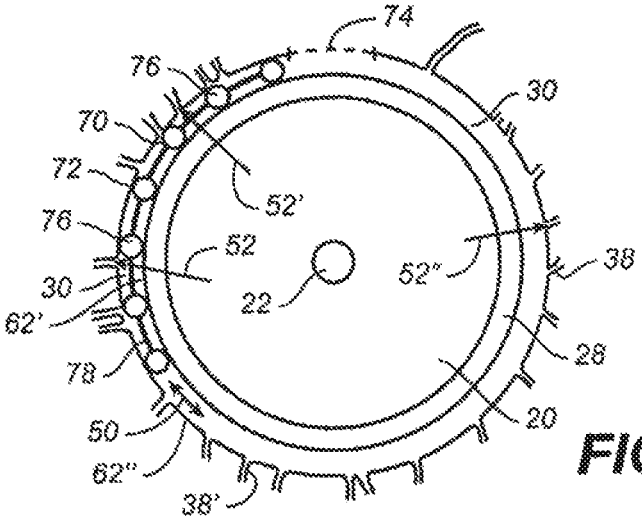

FIG. 5B

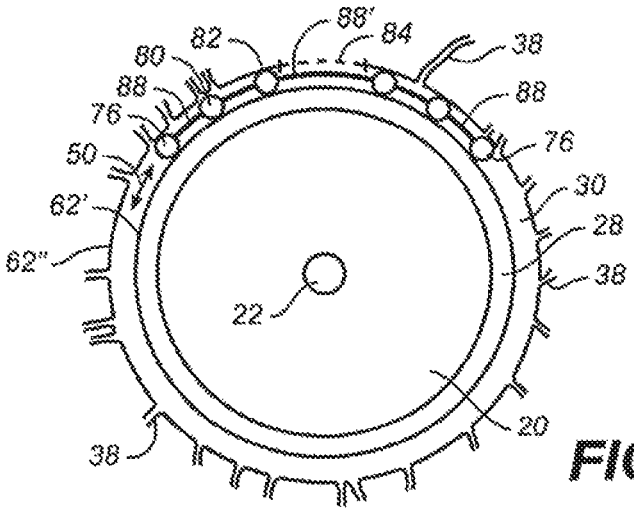

FIG. 5C

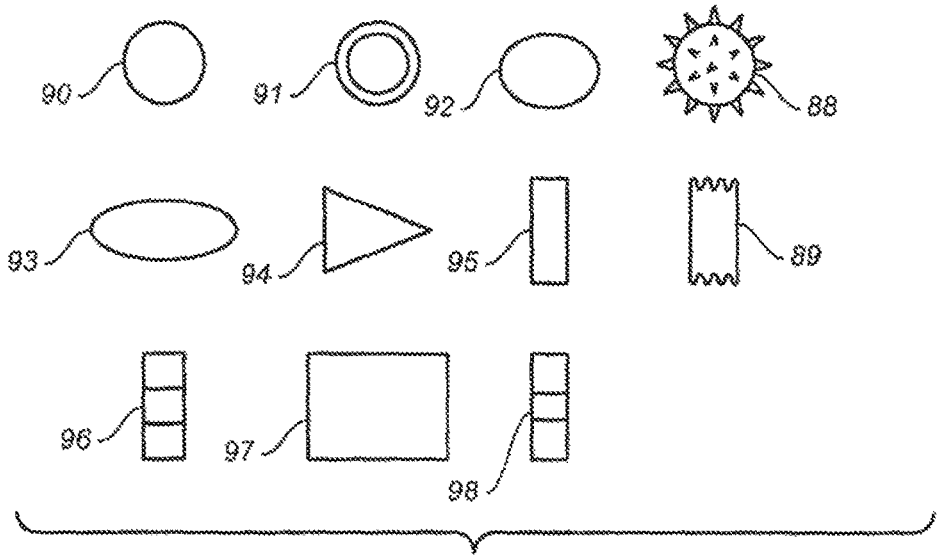

FIG. 6A

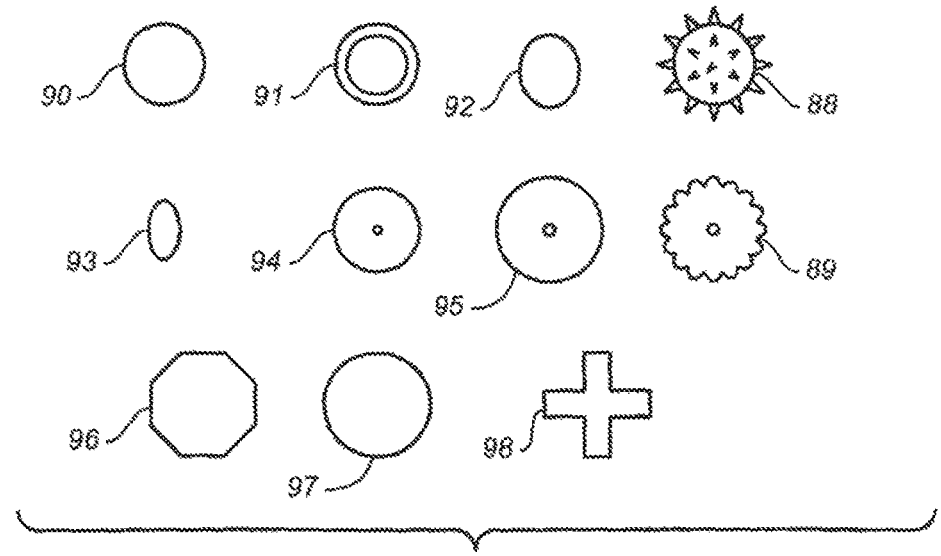

FIG. 6B

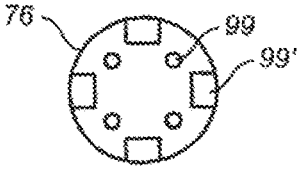

FIG. 6C

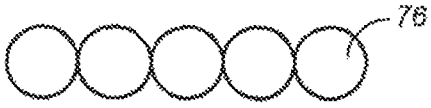

FIG. 7A

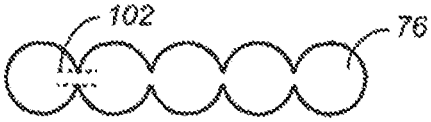

FIG. 7B

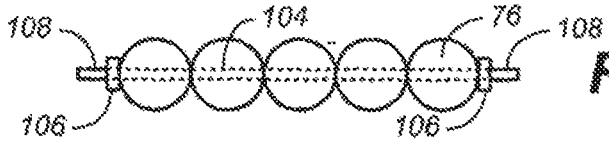

FIG. 7C

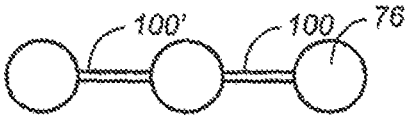

FIG. 7D

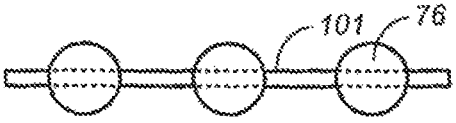

FIG. 7E

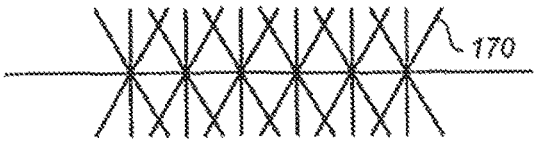

FIG. 8A

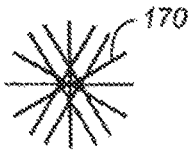

FIG. 8B

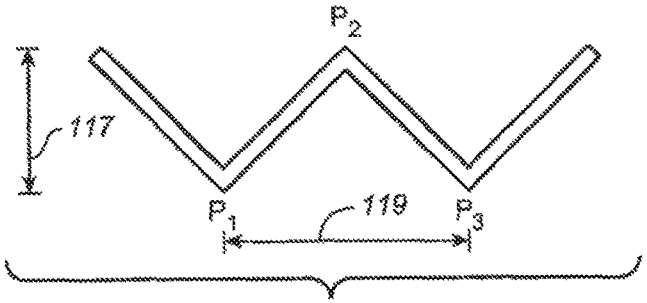

FIG. 8C

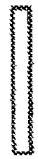

FIG. 8D

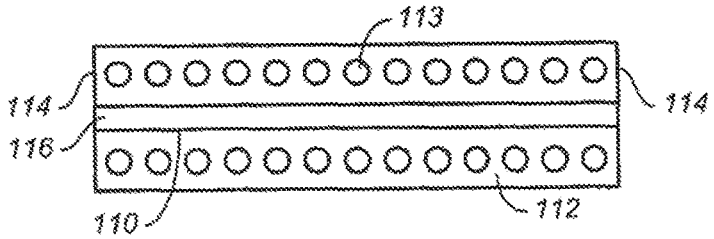

FIG. 8E

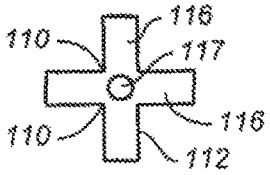

FIG. 8F

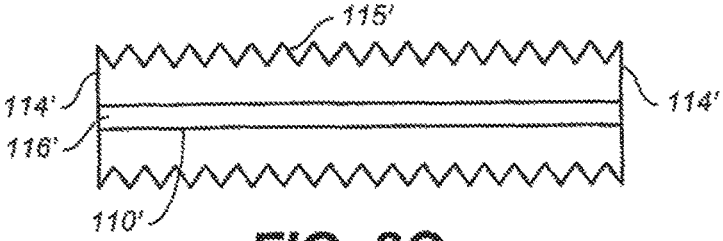

FIG. 8G

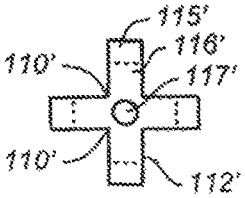

FIG. 8H

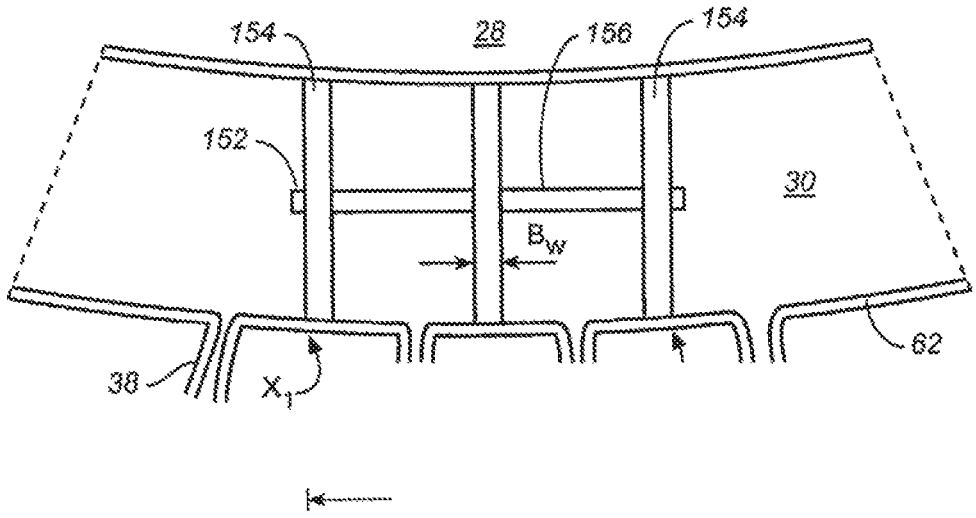
154
28
156
154
152
30
B_W
38
X_1
62

FIG. 9A

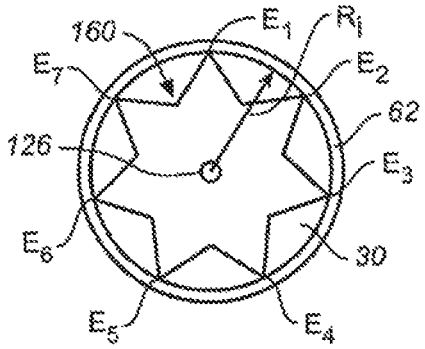
160
E_1
R_1
E_7
E_2
62
126
E_3
E_6
30
E_5
E_4

FIG. 9B

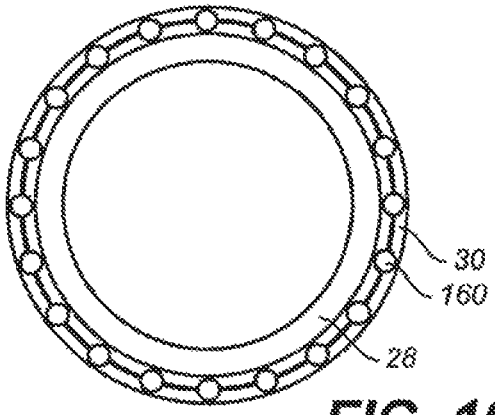

FIG. 10A

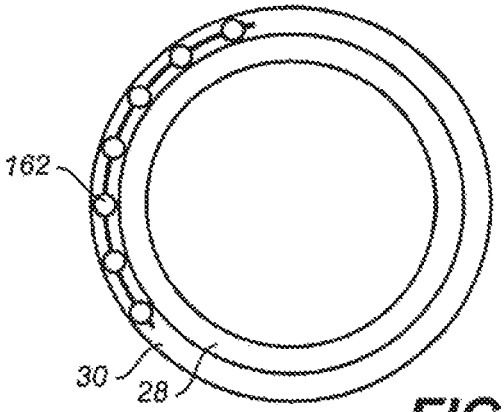

FIG. 10B

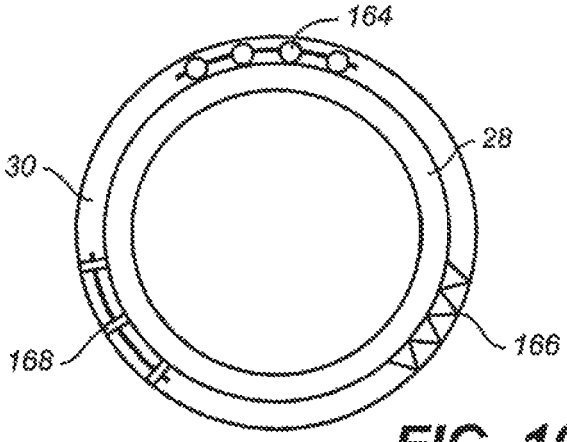

FIG. 10C

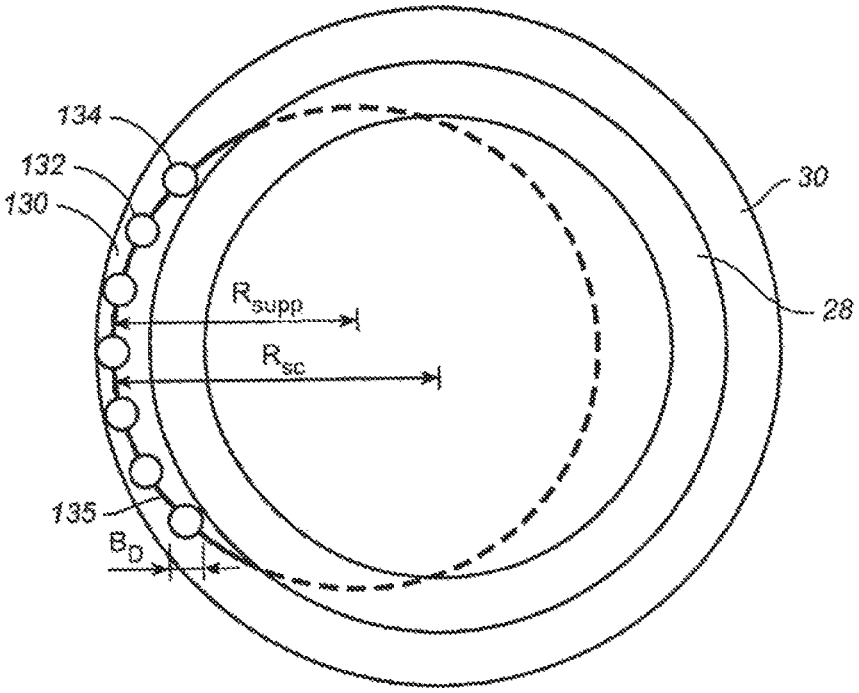

FIG. 11A

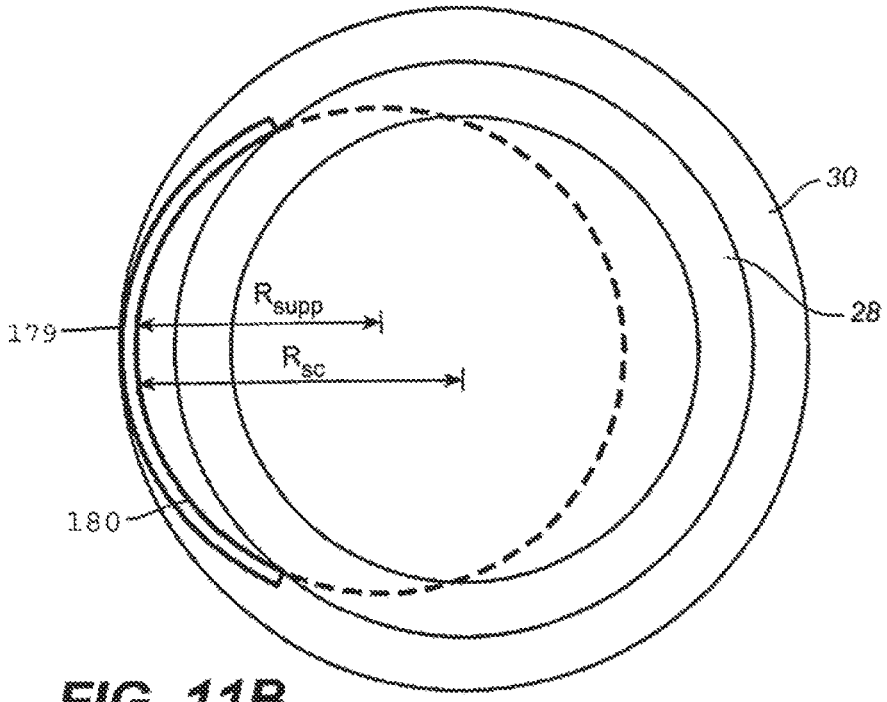

FIG. 11B

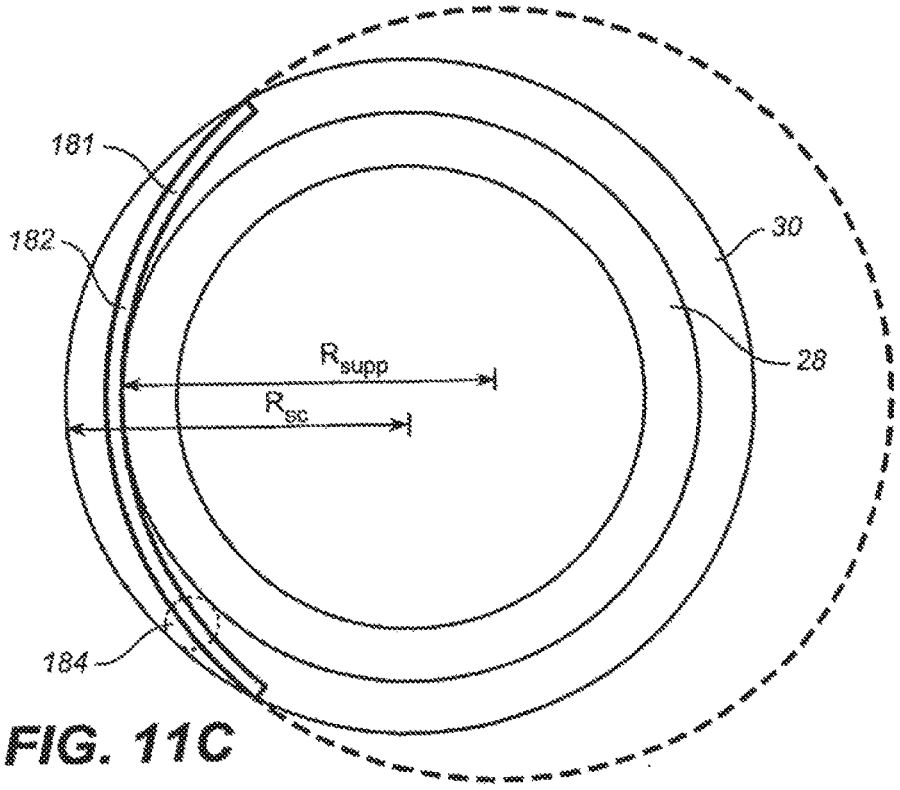

FIG. 11C

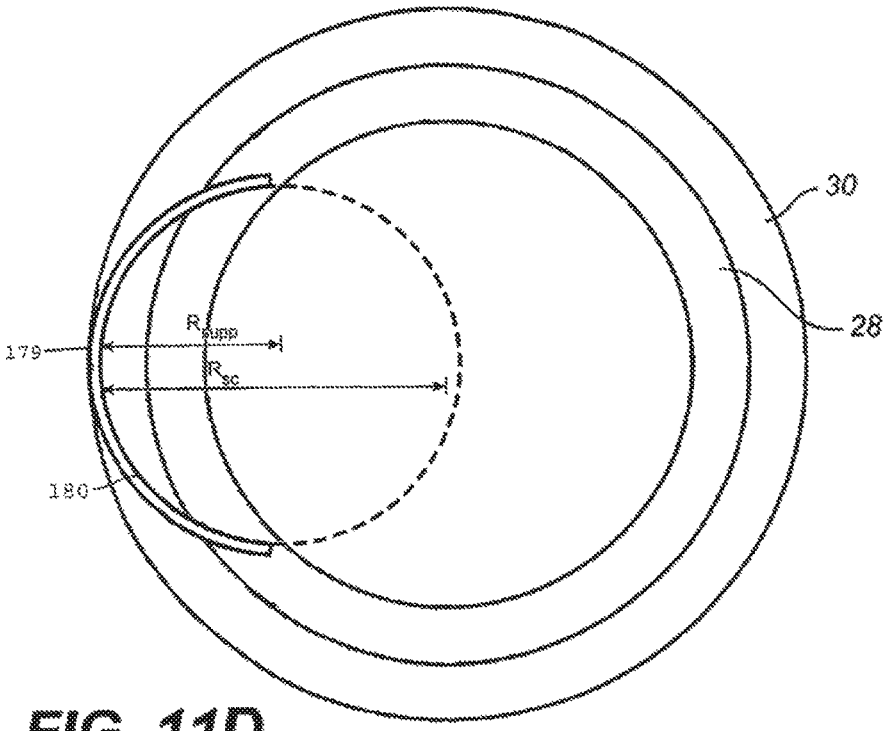

FIG. 11D

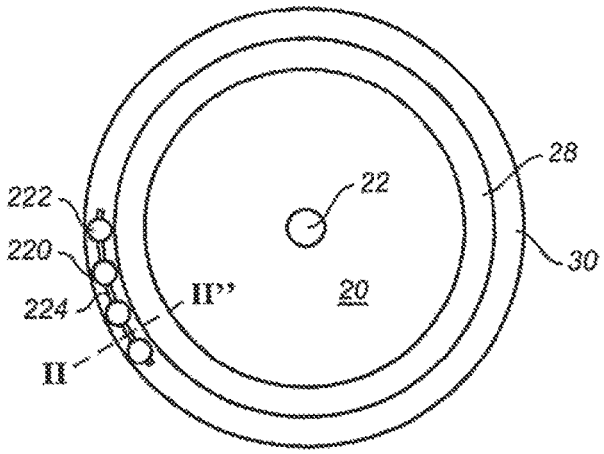

FIG. 12A

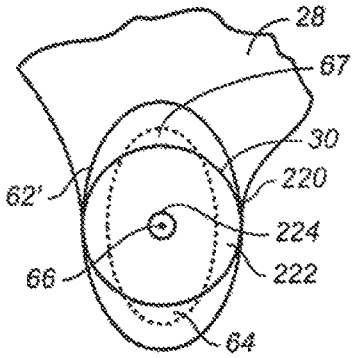

FIG. 12B

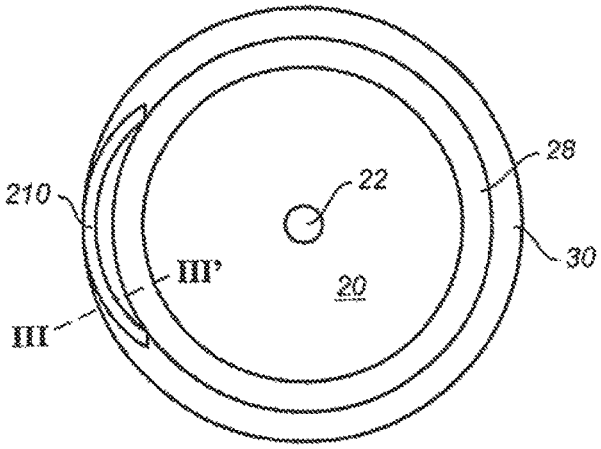

FIG. 12C

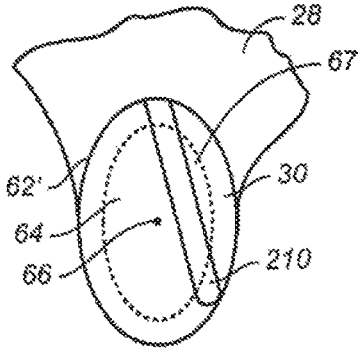

FIG. 12D

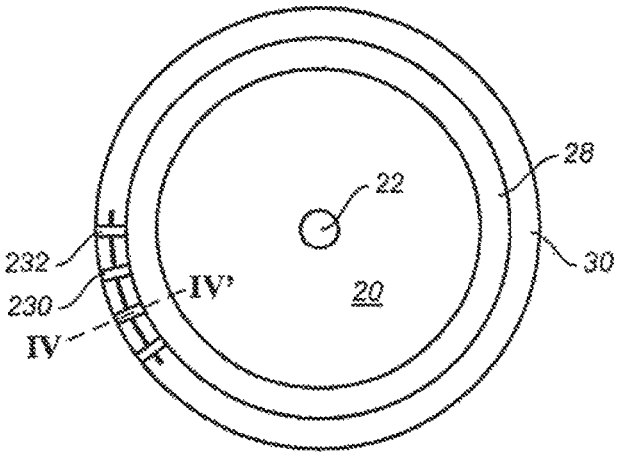

FIG. 12E

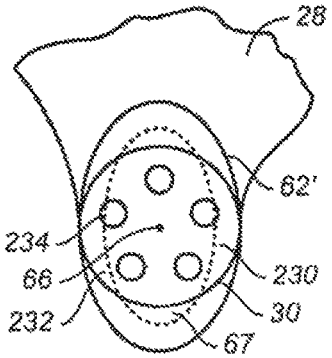

FIG. 12F

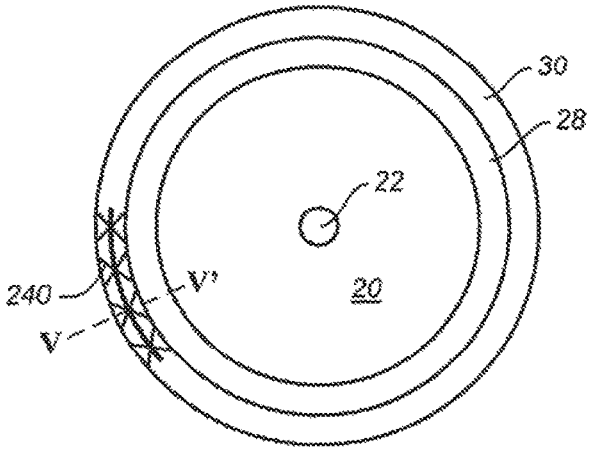

FIG. 12G

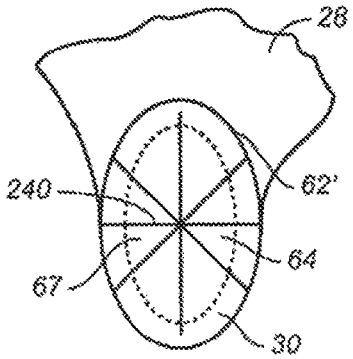

FIG. 12H

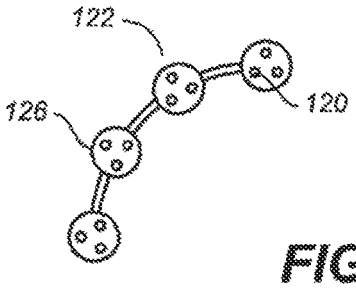

FIG. 13

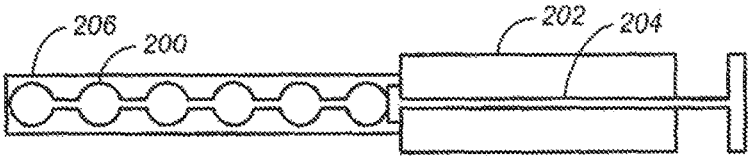

FIG. 14A

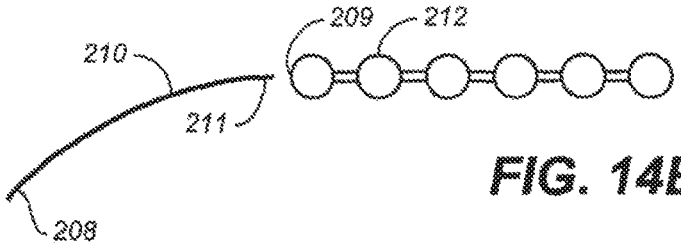

FIG. 14B

FIG. 14C

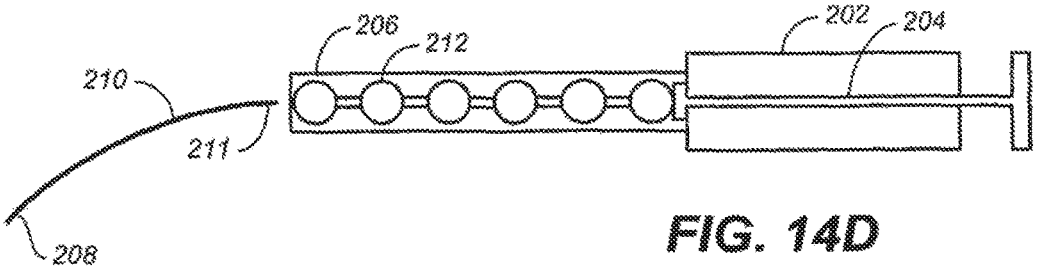

FIG. 14D

INTRAOCULAR IMPLANTS AND METHODS AND KITS THEREFOR

CROSS-REFERENCE TO RELATED APPLICATIONS

This application is a continuation of U.S. patent application Ser. No. 13/025,112, filed Feb. 10, 2011, now issued as U.S. Pat. No. 9,370,443, which is a divisional of U.S. patent application Ser. No. 11/475,523, filed Jun. 26, 2006, now issued as U.S. Pat. No. 7,909,789, each of which is hereby incorporated by reference in its entirety.

FIELD

The devices, kits and methods described herein relate generally to intraocular pressure reduction. More particularly, the devices, kits and methods relate to intraocular implants implantable into Schlemm's canal that can reduce intraocular pressure without substantially interfering with fluid flow across Schlemm's canal.

BACKGROUND

Glaucoma is a potentially blinding disease that affects over 60 million people worldwide, or about 1-2% of the population. Typically, glaucoma is characterized by elevated intraocular pressure. Increased pressure in the eye can cause damage to the optic nerve which can lead to loss of vision if left untreated. Consistent reduction of intraocular pressure can slow down or stop progressive loss of vision associated with glaucoma. In addition, patients are often diagnosed with pre-glaucoma and ocular hypertension when they exhibit symptoms likely to lead to glaucoma, such as somewhat elevated intraocular pressure, but do not yet show indications of optic nerve damage. Treatments for glaucoma, pre-glaucoma and ocular hypertension primarily seek to reduce intraocular pressure.

Increased intraocular pressure is caused by sub-optimal efflux or drainage of fluid (aqueous humor) from the eye. Aqueous humor or fluid is a clear, colorless fluid that is continuously replenished in the eye. Aqueous humor is produced by the ciliary body, and then flows out primarily through the eye's trabecular meshwork. The trabecular meshwork extends circumferentially around the eye at the anterior chamber angle, or drainage angle, which is formed at the intersection between the peripheral iris or iris root, the anterior sclera or scleral spur and the peripheral cornea. The trabecular meshwork feeds outwardly into Schlemm's canal, a narrow circumferential passageway generally surrounding the exterior border of the trabecular meshwork. Positioned around and radially extending from Schlemm's canal are aqueous veins or collector channels that receive drained fluid. The net drainage or efflux of aqueous humor can be reduced as a result of decreased facility of outflow, decreased outflow through the trabecular meshwork and canal of Schlemm drainage apparatus, increased episcleral venous pressure, or possibly, increased production of aqueous humor. Flow out of the eye can be restricted by blockages or constriction in the trabecular meshwork and/or Schlemm's canal.

Glaucoma, pre-glaucoma and ocular hypertension currently can be treated by reducing intraocular pressure using one or more modalities, including medication, incisional surgery, laser surgery, cryosurgery, and other forms of surgery. In the United States, medications or medical therapy are typically the first lines of therapy. If medical therapy is not sufficiently effective, more invasive surgical treatments may be used. In other countries, such as those with socialized medical systems or with nationalized health care systems, surgery may be the first line of therapy if it is considered a more cost effective treatment.

A standard incisional surgical procedure to reduce intraocular pressure is trabeculectomy, or filtration surgery. This procedure involves creating a new drainage site for aqueous humor. Instead of naturally draining through the trabecular meshwork, a new drainage pathway is created by removing a portion of sclera and trabecular meshwork at the drainage angle. This creates an opening or passage between the anterior chamber and the subconjunctival space that is drained by conjunctival blood vessels and lymphatics. The new opening may be covered with sclera and/or conjuctiva to create a new reservoir called a bleb into which aqueous humor can drain. However, trabeculectomy carries both long and short term risks. These risks include blockage of the surgically-created opening through scarring or other mechanisms, hypotony or abnormally low intraocular pressure, expulsive hemorrhage, hyphema, intraocular infection or endophthalmitis, shallow anterior chamber angle, and others. Alternatives to trabeculectomy are actively being sought.

Bypass stents are also used to bridge a blocked trabecular meshwork. Stents can be inserted between the anterior chamber of the eye and Schlemm's canal, bypassing the trabecular meshwork. However, it is difficult to consistently and reliably implant a bypass stent from the anterior chamber into Schlemm's canal. The implant procedure is challenging and stents can become clogged and lose functionality over time. Others have inserted tubular elongated cylindrical hollow stents longitudinally into Schlemm's canal. Cylindrical hollow stents can be configured to allow circumferential fluid flow around the canal. These too can lose functionality over time as a result of occlusion or scarring.

Schlemm's canal is small, approximately 190-370 microns in cross-sectional diameter, and circular. Therefore, it can be difficult or expensive to design and manufacture hollow tubular stents of appropriate dimensions for use in opening Schlemm's canal. In addition, hollow tubular stents can be prone to failure and collapse or occlusion over time, as has been shown for cardiovascular stents. Hollow tubular stents incorporating thin walls are especially prone to failure. Further, the walls of tubular stents placed lengthwise along Schlemm's canal can have significant surface area contact with the trabecular meshwork and/or the collector channels, which can result in blockage of the meshwork or collector channels, substantially interfering with transmural flow across Schlemm's canal and into the eye's collector channels.

Therefore, easily manufacturable, minimally invasive devices for effective, long-term reduction in intraocular pressure are desirable. In addition, methods and kits incorporating such devices are desirable.

SUMMARY

Described here are devices, kits and methods for reducing intraocular pressure. The devices for reducing pressure within the eye comprise a support implantable circumferentially within Schlemm's canal that is configured to maintain the patency of at least a portion of the canal. The support occupies at least a portion of a central core of Schlemm's canal. The support does not substantially interfere with transmural flow across Schlemm's canal, and thereby uti-

lizes the eye's natural drainage pathways. The support can be implanted into Schlemm's canal with minimal trauma to the eye.

The support generally comprises a biocompatible material. At least a portion of the support can be made from a biocompatible polymer, e.g., acrylics, silicones, polymethylmethacrylate, or a hydrogel. In addition, at least part of the support can be made from a biocompatible metal such as gold. In some variations, at least a portion of the support is made from a shape memory material. Suitable shape memory materials include shape memory polymers or shape memory alloys, such as nickel titanium alloys. If a shape memory material is used, the support can have a compressed state prior to and during implantation into Schlemm's canal, and an expanded state following implantation to open the canal.

In some variations, the support is at least partially made from a biocompatible, biodegradable polymer. The biodegradable polymer can be collagen, a collagen derivative, a poly(lactide); a poly(glycolide); a poly(lactide-co-glycolide); a poly(lactic acid); a poly(glycolic acid); a poly(lactic acid-co-glycolic acid); a poly(lactide)/poly(ethylene glycol) copolymer; a poly(glycolide)/poly(ethylene glycol) copolymer; a poly(lactide-co-glycolide)/poly(ethylene glycol) copolymer; a poly(lactic acid)/poly(ethylene glycol) copolymer; a poly(glycolic acid)/poly(ethylene glycol) copolymer; a poly(lactic acid-co-glycolic acid)/poly(ethylene glycol) copolymer; a poly(caprolactone); a poly(caprolactone)/poly(ethylene glycol) copolymer; a polyorthoester; a poly(phosphazene); a poly(hydroxybutyrate) or a copolymer including a poly(hydroxybutyrate); a poly(lactide-co-caprolactone); a polycarbonate; a poly(esteramide); a polyanhydride; a poly(dioxanone); a poly(alkylene alkylate); a copolymer of polyethylene glycol and a polyorthoester; a biodegradable polyurethane; a poly(amino acid); a polyetherester; a polyacetal; a polycyanoacrylate; a poly(oxyethylene)/poly(oxypropylene) copolymer; and blends and copolymers thereof.

The support can comprise an active agent. For example, a support can be coated or impregnated with an active agent. Alternatively, an active agent can be dispersed within the support, e.g., by filling a cavity within the support. The active agent can include a prostaglandin, a prostaglandin analog, a beta blocker, an alpha-2 agonist, a calcium channel blocker, a carbonic anhydrase inhibitor, a growth factor, an anti-metabolite, a chemotherapeutic agent, a steroid, an antagonist of a growth factor, or combinations thereof. The release of the active agent can be controlled using a time release system, e.g., by embedding or encapsulating the active agent with a time release composition.

In some variations, the support will be solid. In other variations, at least a portion of the support will be hollow or porous. The surface of the support may be smooth, rough, spiked, or fluted. In still other variations, at least part of the support will be made from mesh. The support can include at least one fenestration and one or more rod-like members.

In some variations, the support comprises at least two adjacent beads. Adjacent beads can have the same or different sizes and shapes, and can be made from the same or different materials. The bead shapes can be spherical, spheroid, ovoid, cylindrical, cuboid, cubical, conical, discoid, helical, or segments thereof. In some variations, there is a connector linking at least two adjacent beads together. If there is a connector, it can be rigid or flexible. If there is more than one connector, e.g., two connectors inserted between three beads, the connectors may be of the same or different lengths. The connectors can include the same or different material as the beads they connect. A connector can also function as a spacer configured to provide space between adjacent beads. In some variations, the support comprises at least two discs separated by, and connected with, a connector. The discs may include fenestrations. The connector may also comprise a guide wire over which a fenestrated bead can be threaded into the canal of Schlemm.

The support can extend approximately all the way around Schlemm's canal, if the support has a circumference approximately equal to the circumference of Schlemm's canal. Alternatively, the support can extend only about half way around the circumference of Schlemm's canal, or about a quarter way around the canal. In some variations, the support will extend less than a quarter circumference of Schlemm's canal. The support can be configured to contact the inner surface of the wall of Schlemm's canal at two, three or more points. In some variations, the support can be attached to tissue. The support may comprise a stiff arcuate member having a radius of curvature smaller or larger than that of Schlemm's canal.

In some variations, the support can be altered using electromagnetic radiation. For example, a laser having a wavelength absorbable by at least one localized portion of the support can be used to alter the support. In other variations, electromagnetic radiation can be used to release an active agent from the support. In still other variations, the support can be visually enhanced using fluorescence or phosphorescence emission. For example, the support can comprise a chromophore that fluoresces or phosphoresces upon excitation with a light source. In some variations, the emitted fluorescence or phosphorescence is in the wavelength range of about 300 nm to about 800 nm. In some variations, the support can comprise a chromophore that enhances postoperative monitoring of the support.

Kits for reducing intraocular pressure are also provided. The kits contain a support that can be implanted circumferentially within Schlemm's canal. The support is configured to maintain the patency of at least part of Schlemm's canal. The support occupies at least a portion of a central core of Schlemm's canal and does not substantially interfere with transmural flow across the canal. The kits also contain an introducer for implanting the support within the canal. In some variations, the kits include a positioning device for adjusting the support within the canal. In other variations, kits include instructions. In still other variations, the kits include an active agent. Some kits contain at least two supports. If more than one support is included, the kits can include at least two introducers for delivering the supports. Multiple supports within the same kit can have the same or different shape, size, or composition. Multiple supports within the same kit can be connected together or remain separate. In some variations, kits include a fixation device for attaching a support to tissue. In other variations, kits may include a system for visually enhancing the appearance of the support.

Methods for reducing intraocular pressure are also described. The methods include inserting a support circumferentially within Schlemm's canal. The support is configured to maintain the patency of at least part of the canal. The support occupies at least a portion of a central core of Schlemm's canal, and does not substantially interfere with transmural flow across the canal. In some variations, the methods also include dilating Schlemm's canal prior to insertion of the support. In still other variations, the methods comprise anchoring the support to tissue. The methods can include implanting at least two supports. If more than one support is implanted within a single eye, the multiple

supports can be positioned circumferentially adjacent to each other or circumferentially opposed (i.e., positioned about 180° apart) to each other within Schlemm's canal. Multiple supports within one eye can be connected or remain separate. In some variations of the methods, the support is illuminated with a light source to visually enhance the position of the support. In other variations of the methods, the support can be altered using electromagnetic radiation. For example, a laser absorbed by at least one localized portion of the support can be used to alter the support. The alteration can comprise the creation or enlargement of an aperture in the support. If electromagnetic radiation is used to alter a support, the alteration can occur before implantation or after implantation.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. **1** provides a partial cross-sectional side view of a normal human eye.

FIG. **2** provides a partial cross-sectional side view of a normal drainage path of fluid from the eye.

FIG. **3** shows a front view of normal fluid drainage from the eye.

FIG. **4**A shows an alternative front view of normal fluid drainage paths from the eye. FIG. **4**B shows a cross-sectional view along line I-I'.

FIG. **5**A provides a front view of an eye in which Schlemm's canal is narrowed or collapsed. FIG. **5**B shows a front view of a device including a support inserted into Schlemm's canal that allows transmural flow across the canal. FIG. **5**C illustrates an alternate design for a device inserted into Schlemm's canal that allows transmural flow across the canal.

FIG. **6**A shows side views of various element or bead configurations that can be used in the supports described herein. FIG. **6**B shows the corresponding front views of the element or bead configurations shown in FIG. **6**A. FIG. **6**C illustrates an element or bead having fenestrations.

FIG. **7**A illustrates a support having multiple juxtaposed beads. FIG. **7**B illustrates a support having multiple juxtaposed and connected beads. FIG. **7**C shows an alternate configuration of a support having multiple juxtaposed and connected beads. FIG. **7**D shows a support having multiple, spaced-apart but connected beads. FIG. **7**E illustrates beads threaded onto a connector.

FIGS. **8**A-B show side and front views, respectively, of a support having an open network structure. FIGS. **8**C-D show side and front views, respectively, of a support having a longitudinal zig-zag configuration that will contact the wall of Schlemm's canal at at least three points (labeled P_1, P_2, P_3). FIGS. **8**E-F show side and front views, respectively, of a support having a rod-like member with continuously fluted edges and fenestrations. FIGS. **8**G-H show side and front views, respectively, of another variation of a support having a rod-like member with continuously fluted edges.

FIGS. **9**A-B show expanded cross-sectional views of a support implanted within Schlemm's canal.

FIGS. **10**A-C illustrate various configurations of supports implanted into Schlemm's canal.

FIGS. **11**A-B and D illustrate configurations of supports having a smaller radius of curvature then Schlemm's canal. FIG. **11**C shows a support having a larger radius of curvature than Schlemm's canal.

FIG. **12**A illustrates a variation of a support traversing the center of the central core of Schlemm's canal. FIG. **12**B shows a cross-sectional view along line II-II'. FIG. **12**C illustrates a variation of a support traversing the central core of the canal. FIG. **12**D shows a cross-sectional view along line III-III'. FIG. **12**E illustrates a variation of a support that occupies the majority of the central core of the canal. FIG. **12**F shows a cross-sectional view along line IV-IV'. FIG. **12**G illustrates a variation of support having an open network that occupies a portion of the central core of the canal. FIG. **12**H shows a cross-sectional view along line V-V'.

FIG. **13** shows an illustrative example of a support that can be modified using electromagnetic radiation.

FIG. **14**A illustrates a syringe that can be used to insert a support into Schlemm's canal. FIG. **14**B illustrates a variation in which a support is threaded onto a guide element for insertion and positioning in Schlemm's canal. FIG. **14**C illustrates a cross-sectional view of a support having a central bore to accommodate a guide element. FIG. **14**D illustrates a variation in which a syringe and a guide element are used for insertion and positioning of a support in Schlemm's canal.

DETAILED DESCRIPTION

Described here are devices, kits and methods to reduce intraocular pressure by maintaining or restoring Schlemm's canal so that at least a portion of the canal is patent or unobstructed. The devices, kits and methods operate to keep Schlemm's canal from collapsing while not substantially interfering with the eye's natural drainage mechanism for aqueous humor, in which transmural fluid flow across Schlemm's canal occurs. The devices are implantable in Schlemm's canal with minimal trauma to the eye.

With reference to the figures, FIG. **1** shows a partial cross-sectional view of the anatomy of a normal human eye. Ciliary body **12** is connected to iris **18** and to lens **16** via zonular fibrils **14**. The anterior chamber of the eye **20** is bounded on its anterior (front) surface by cornea **24**. In the center of iris **18** is pupil **22**. Cornea **24** is connected on its periphery to sclera **26**, which is a tough fibrous tissue forming the white shell of the eye. Trabecular meshwork **28** is located on the outer peripheral surface of anterior chamber **20**. The trabecular meshwork extends 360° circumferentially around the anterior chamber. Located on the outer peripheral surface of meshwork **28** is Schlemm's canal **30**. Schlemm's canal extends 360° circumferentially around the trabecular meshwork. At the apex formed between iris **18**, meshwork **28** and sclera **26** is angle **32**. Conjunctiva **34** is a membrane overlaying sclera **26** and lining the inside of the eyelid (not shown).

FIG. **2** shows a partial cross-sectional view of flow of aqueous humor within and out of a normally functioning human eye. Aqueous humor is produced in ciliary body **12** and its path through and out of the eye is indicated by solid directional line **36**. The aqueous humor flows from ciliary body **12**, between lens **16** and iris **18**, through pupil **22** into anterior chamber **20**, across trabecular meshwork **28**, across Schlemm's canal **30**, into aqueous veins or collector channels (not shown) and finally into the bloodstream via conjunctival vasculature.

FIG. **3** shows a front view of normal flow of aqueous humor out of the eye. Aqueous humor enters anterior chamber **20** via pupil **22**. The fluid flows outwardly toward the periphery of the eye, with the general path of flow indicated by solid directional lines **36**. The fluid crosses trabecular meshwork **28** and traverses Schlemm's canal **30** to reach aqueous veins or collector channels **38**. There are typically 25-30 collector channels located in a human eye. Collector channels **38** are connected to vasculature **40**, whereby the drained aqueous humor enters the bloodstream. Although

the direction of net or bulk fluid flow is depicted as radially outward by directional lines **36** from pupil **22** for simplicity, actual fluid flow in an eye may follow more varied paths.

Different fluid flow paths in and across Schlemm's canal are illustrated in FIGS. **4**A-B. FIG. **4**A shows a front view of an eye, and FIG. **4**B shows an expanded cross-sectional view along line I-I'. Circumferential (i.e., longitudinal) flow along and around circular canal **30** is depicted by directional lines **50**. Fluid that does not traverse canal **30** to reach collector channels **38** may not be effectively drained from the eye. Examples of fluid flow paths that can effectively drain the eye are illustrated by directional lines **52**, **52'**, and **52"**. In each of these paths, fluid enters trabecular meshwork **28** along its inner peripheral surface **60** and exits the meshwork along its outer peripheral surface **62'**. Meshwork outer peripheral surface **62'** provides the inner peripheral surface or wall of Schlemm's canal **30**. Transmural fluid flow across Schlemm's canal involves two instances of transmural flow across walls or boundaries. First, fluid must flow from trabecular meshwork **38** through inner peripheral surface or wall **62'** of Schlemm's canal **30** to reach lumen **64** of the canal. Second, fluid must flow from lumen **64** through canal outer peripheral wall **62"** through apertures **38'** to enter collector channels **38**. Finally, the collector channels **38** feed the drained fluid into vasculature. Lumen **64** of canal **30** includes a central core region **67**. Thus, fluid flow from the eye differs from fluid flow in other vessels in the body where fluid need only flow longitudinally along the vessel, such as blood flowing through a vein.

Devices

Devices to reduce intraocular pressure comprising a support that can be implanted circumferentially in Schlemm's canal to maintain the patency of at least a portion of the canal are described here. The support occupies at least a portion of a central core of Schlemm's canal and does not substantially interfere with transmural flow across the canal. By "maintain the patency" of at least a portion the canal, it is meant that the support operates to keep the canal at least partially unobstructed to transmural flow, such that fluid can 1) exit through the trabecular meshwork; 2) traverse the canal; and 3) drain via the collector channels. To maintain the patency of the canal, it is not necessary that the support leave the canal unobstructed in regard to circumferential flow. By "does not substantially interfere" with transmural flow, it is meant that the support does not significantly block either fluid outflow from the trabecular meshwork or fluid outflow to the collector channels. In many variations, the support allows between about 0.1 and about 5 microliters per minute aqueous outflux from the eye through the trabecular meshwork and collector channels. The "central core of Schlemm's canal" refers to the region around the cross-sectional center of the canal in the interior space of the canal lumen, i.e., not on the periphery of the canal. Therefore, a device that occupies at least a portion of a central core of Schlemm's canal can traverse at least a portion of the canal's lumen.

Therefore, devices described here need not comprise an open-ended tubular support placed longitudinally along Schlemm's canal, i.e., the devices and supports can be non-tubular. A longitudinal, open-ended tubular support can enable longitudinal flow along the canal. However, even if fluid can flow longitudinally (i.e., circumferentially) along Schlemm's canal, the eye may not be effectively drained unless the fluid eventually traverses the canal. That is, transmural fluid flow across two boundaries must occur: 1) fluid must flow from the trabecular meshwork through a canal inner wall coincident with an outer peripheral boundary of the trabecular meshwork to reach the canal lumen; and 2) fluid must flow from the canal lumen through apertures in the canal outer peripheral wall to reach the connector channels. The collector channels are then able to further disperse the fluid and complete the natural draining process. A tubular support inserted longitudinally into the canal can have significant surface area overlap with surfaces of the canal such that transmural flow across the canal may be significantly impeded. A longitudinal tubular support placed in Schlemm's canal may block flow into the canal from the trabecular meshwork and block flow out of the canal into the collector channels.

Devices described herein for treating elevated intraocular pressure include a support that is implanted within Schlemm's canal. In many instances, the device will reduce the intraocular pressure by 1-40 mm Hg, for example by at least 2 mm Hg. In other instances, the device will reduce intraocular pressure by at least 4 mm Hg, or at least 6 mm Hg, or at least 10 or 20 mm Hg. In still other instances, the device will operate to bring the intraocular pressure into the range of about 8 to about 22 mm Hg. The support can be configured in a variety of ways to at least partially prop open Schlemm's canal thereby maintaining its patency without substantially interfering with or impeding transmural fluid flow across Schlemm's canal. In some variations, the support may interfere with or block longitudinal flow along or around the canal. In many instances, the support will be contained entirely within Schlemm's canal. In some variations the support will be implanted within the canal, but may extend partially beyond Schlemm's canal, e.g., into the trabecular meshwork.

In some variations, a support to maintain at least partial patency for Schlemm's canal to enable fluid flow between an inner wall of the canal and an outer wall of the canal can comprise elements or structures such as bead-like elements or beads, which can be connected together, e.g., as a string of beads. Individual elements or beads or a connected group of elements or beads can be inserted directly into Schlemm's canal. A more detailed description of supports incorporating elements or beads is provided below.

FIG. **5**A illustrates a front view of an eye having a narrowed or collapsed Schlemm's canal **30**, where canal outer peripheral wall **62"** is very close to canal inner peripheral wall **62'**. Although Schlemm's canal **30** is depicted in FIG. **5**A as being uniformly narrow around the entire circumference of canal, it is possible that only a portion of Schlemm's canal is narrowed or collapsed. When Schlemm's canal is collapsed or narrowed, net efflux of aqueous from the anterior chamber to the collector channels **38** is diminished, thereby increasing intraocular pressure. As a result, the risk of pre-glaucoma, ocular hypertension, or glaucoma can increase.

FIG. **5**B illustrates an example of a device **70** inserted into Schlemm's canal **30** through incision site **74**. Device **70** in this example is positioned to one side of incision site **74**. Device **70** includes support **72** that is configured to keep Schlemm's canal at least partially open to transmural fluid flow across both canal inner wall **62'** and canal outer wall **62"** to reach collector channels **38** via apertures **38'**. In the example shown in FIG. **5**B, support **72** includes elements or beads **76** connected with connectors **78**. In this variation, the distance between canal inner wall **62'** and outer wall **62"** is approximately determined by the cross-sectional dimension of support **72**, which is in turn determined by the largest cross-sectional diameter of the beads **76**. Therefore, circumferential (i.e., longitudinal) fluid flow around and along the canal **30** indicated by directional line **50** may be inhibited by

the insertion of support **72** into the canal. However, transmural flow across both walls or boundaries of the canal indicated by directional lines **52**, **52'**, **52"** is enhanced by support **72** and fluid is able to reach collector channels **38** and be drained from the eye. As a result, support **72** can effectively reduce intraocular pressure by utilizing the eye's natural drainage mechanism. Incision **74** need only be large enough to accommodate the diameter of beads **76**, so that trauma to the eye is minimized. Beads can have cross-sectional dimensions in the range from about 50 microns to about 500 microns. Insertion of beads having relatively small cross-sectional diameters (e.g., about 50 microns) into Schlemm's canal open the canal less than the normal cross-sectional diameter of the canal, which is about 190 to about 370 microns, but still can maintain the patency of the canal. Insertion of beads having relatively large cross-sectional diameters (e.g., greater than about 300 microns) can open the canal as large as or larger than the canal's normal cross-sectional diameter and also can operate to stretch the trabecular meshwork. Stretching the trabecular meshwork may further enhance drainage.

FIG. **5**C illustrates an alternate configuration of a device **80** inserted into Schlemm's canal **30** through incision site **84**. Device **80** includes support **82** that extends to both sides of incision site **84**. Support **82** includes elements or beads **76** connected with connectors **88** and **88'**. In this example, connector **88'** is of a different length than connectors **88**. As in FIG. **5**B, beads **76** may impede circumferential (i.e., longitudinal) fluid flow around and along canal **30** indicated by directional line **50**. However transmural flow across the canal is enhanced by support **82** that maintains patency across the canal and allows fluid to reach collector channels **38**. If the beads are fenestrated or comprise rough, spiked, or fluted perimeters, then circumferential fluid flow through or around the beads may also occur.

Elements or beads used in a support may be hollow and closed structures, open structures, solid structures, porous structures, or any combination thereof, and may be of any suitable shape. FIGS. **6**A and **6**B illustrate side and front views, respectively, of exemplary elements or beads that may be used in the supports described here. As shown, solid **90** or hollow **91**, spherical **90**, spheroid **92**, ovoid **93**, conical **94**, disk-shaped **95**, polyhedral **96**, rod-like **97**, or beads with fluted edges **98**, rough edges, **89**, or spiked edges **88** may be used. In some instances, it may be desired to round corners or edges of the beads. As illustrated in FIG. **6**C, elements or beads **76** may include fenestrations **99**, **99'**. Fenestrations may have any suitable cross-sectional shape, such as round or quadrilateral. Although a disc-shaped bead **76** is shown in FIG. **6**C, any shape of bead can be fenestrated.

As illustrated in the variations shown in FIGS. **7**A-E, two or more beads **76** in a support may be adjacent to each other. Adjacent beads may be juxtaposed (FIG. **7**A), connected and juxtaposed (FIGS. **7**B and **7**C), or connected together with connectors **100**, **100'** to form intervals between beads (FIG. **7**D). In addition, beads may be threaded onto a connector **101** (FIG. **7**E). Multiple beads used in a single support may have the same or different shapes, and may be made of the same or different materials.

Junctions **102** between beads as shown in FIG. **7**B can be made using any suitable technique, such as by using an adhesive, chemical bonding, mechanical interlocking, or welding. Beads may also be juxtaposed and connected as shown in FIG. **7**C by threading onto a guide element **104**. Guide element **104** can comprise a fiber, a suture, a guide wire, a fixture, or the like. The beads can be fixed in a juxtaposed configuration on a guide element, e.g., by knotting ends of the fiber or by providing other end-blocking devices **106**, such as clips, caps, protrusions, or the like on ends **108** of element **104**. Any or all of the beads can be attached to guide element **104**, e.g., beads occupying end positions may be attached to element **104** and function as blocking beads to keep beads from sliding off ends **108** of element **104**. Alternatively, beads may slide along element **104**. Guide element **104** can be flexible, such as thin polymer threads, such as a suture, or metal wires. Alternatively, element **104** can be flexible but fixable, such as one or more shapeable metal wires that can be bent into a desired position and maintain that position against some amount of external stress or pressure. In other variations, guide element **104** can be rigid, e.g., a molded polymeric piece or a stiff metal piece.

As shown in FIG. **7**D, multiple connectors **100**, **100'** may be used in a single support, with at least one connector inserted between adjacent beads **76**. If multiple connectors are used, they may be of the same or different lengths. In addition, multiple connectors within the same support may be made of the same or different materials, and the connectors may be made of the same or different materials than the beads. Discrete connectors **100**, **100'** can be inserted between beads **76** and attached to adjacent beads using any suitable method including using adhesives, chemical bonding, welding, mechanical interlocking, knots, or any combination thereof. In some variations, connectors **100**, **100'** between beads can be configured to function as spacers between individual beads. As illustrated in FIG. **7**E, beads **76** can also be threaded onto a connector **101**. If the beads are threaded onto a connector, the beads can be maintained in fixed positions along the connector **101** by any suitable method, including using adhesives, chemical bonding, welding, clips, protrusions on the connector, mechanical interlocking locking between a connector and a bead, knots, or any combination thereof. Alternatively, some or all beads may slide along connector **101**. Connectors **100**, **100'**, **101** can be flexible, such as thin polymer threads or metal wires. Connectors **100**, **100'**, **101** can also be flexible but fixable, such as shapeable metal wires. Alternatively, connectors **100**, **100'**, **101** may be rigid, such as molded polymeric connectors or stiff metal connectors.

Supports of the devices described here need not contain beads. For example, a support can be a unitary structure of fixed or variable length. Supports can be solid, hollow, or porous, or any combination thereof. For example, a support can be partially solid and partially hollow. Examples of support configurations are shown in side view and front view in FIGS. **8**A-F. As illustrated in FIG. **8**A-B, a support can have an open network structure. Such a support can be fabricated out of shapeable metal wires, for example. The support illustrated in FIGS. **8**A-B will have minimal surface area contact with the walls of Schlemm's canal, i.e., only point contacts at the end of wires or fibers **170**. Alternatively, a support having an open network structure can be at least partially made from a mesh or foam. The mesh or foam can be made of any suitable material, e.g., metal or plastic. As shown in FIGS. **8**C-D, the support can have a sinusoidal or zig-zag configuration extending along a selected length of Schlemm's canal. For the example shown in FIG. **8**C, the support will contact the wall of Schlemm's canal at at least three points, labeled P_1, P_2, and P_3, after implantation. In FIGS. **8**E-H, examples of rod-like supports having fluted edges are shown. In FIGS. **8**E-F, fluted edges **110** extend longitudinally along sides **112** between ends **114** of the support to form structures **116**. Structures **116** can include fenestrations **113**. The support can include central bore **117**. In FIGS. **8**G-H, fluted edges **110'** extend along sides **112'** to

form structures **116'**. Structures **116'** have serrated outer surfaces **115'** extending between ends **114'**. The support can include central bore **117'**. In the variations illustrated in FIGS. **8**E-H, the support may contact the canal walls at at least four points. In some variations, the support is adjustable.

A common characteristic of the support configurations described here is that they need not have continuous or extensive contact with a wall of Schlemm's canal. Indeed, many of the described devices and structures have minimal tangential, periodic, or sporadic contact with the wall. The surface of the support can be rough, smooth, spiked or fluted. As the example shown in FIGS. **8**A-B shows, some supports only have point contacts with the canal wall. For the supports shown in FIGS. **5**B-C, the rounded beads of each of the supports make only tangential contact with the canal wall. Bead shapes can be selected or designed to have minimal surface area contact with canal walls, e.g., beads **98** having fluted edges as shown in FIGS. **6**A-B may have low surface area contact with canal walls. In addition, supports having widely spaced apart beads, e.g., by connectors illustrated in FIGS. **7**D-E that can function to space beads at desired intervals to reduce contact with canal walls yet operate to keep the canal open. As illustrated above with respect to FIGS. **8**C-D, in some variations, the support contacts the interior wall of the canal at at least two points; or at at least three points.

Expanded cross-sectional views of a support **152** implanted circumferentially in Schlemm's canal are provided FIGS. **9**A-B. The fraction of canal wall surface area in contact with a support can be estimated by viewing the inside of Schlemm's canal as a slightly arcuate cylinder C having length L, extending circumferentially from a first end X_1 to a second end X_2 of support **152**, and inside radius R_i. In some variations, the support contacts less than 0.1% or less than 1% of the surface area of the cylinder C as described above. In other variations, the support contacts less than 10% of the surface area of C. In still other variations, the support contacts less than 30% of the surface area of C. For example, the support **152** shown in FIGS. **9**A-B contacts the canal wall **62** only at bead outer peripheral edges at E_1-E_7, along a distance of the bead width B_W. There is no contact with the canal walls where connectors **156** space apart beads **154**, and no contact in fluted regions **160** of beads **154**. The design feature of minimal support contact with canal walls allows a support to maintain patency of the canal without substantially interfering with transmural flow across the canal. If a substantial portion of the surface area of the inner periphery of the canal adjacent to the trabecular network or of the surface area of the outer periphery of the canal where the collector channels are located is blocked, effective fluid flow across the canal may be impaired.

Supports can have variable lengths and thicknesses. For example, the length of supports using beads can be tuned by varying the number, type, or spacing of beads, or any combination thereof. The thickness of a support can be increased by adding one or more beads having larger dimensions. Unitary supports can also be built with varying lengths, or with adjustable (e.g., trimmable) dimensions. For example, for a support made of shapeable metal having a sinusoidal or zig-zag configuration as shown FIGS. **8**C-D, a cross-sectional dimension **117** of the support can be decreased or increased by apply tension along dimension **119**. As illustrated in FIG. **10**A, a support **160** can extend essentially around the entire circumference of Schlemm's canal **30**. Alternatively, a support can extend approximately half way around the circumference of the canal (not shown). As shown in FIG. **10**B, a support **162** can extend less than half way around the canal. As shown in FIG. **10**C, a support **164** can extend a quarter or less of the circumference around the canal. In addition, more than one support **164**, **166**, **168** can be inserted into a single Schlemm's canal. If multiple supports are inserted into a single canal, they can be of different shapes, lengths, materials or sizes.

A support can be configured such that it will open the canal beyond a maximum cross-sectional dimension of the support itself. For example, as illustrated in FIG. **11**A, device **130** comprising support **132** is inserted into Schlemm's canal **30**. Support **132** comprises beads **134** which have a maximum cross-sectional dimension B_D. Support **132** comprises a stiff arcuate element **135** with a radius of curvature R_{supp} smaller than the radius of curvature of Schlemm's canal R_{SC}. The smaller, fixed radius of curvature R_{supp} of arcuate member **135** urges canal **30** to open more than B_D. In other variations shown in FIGS. **11**B and **11**D, support **179** comprises an arcuate member **180** without beads having a radius of curvature R_{supp} that is less than the radius of curvature R_{SC} of the canal. Member **180** is sufficiently stiff to urge the canal open. In another variation shown in FIG. **11**C, support **181** comprises an arcuate member **182** having a radius of curvature R_{supp} larger than that of Schlemm's canal R_{SC}. Member **182** is also sufficiently stiff to urge the canal open. Arcuate members **135**, **180** and **182** can comprise a shape memory material such as Nitinol, for example. As indicated in FIG. **11**C, support **181** can include beads **184**. To urge open the canal, the radius of curvature R_{supp} of an arcuate members can be about 10%, 20%, 30%, 40%, or 50% or smaller or larger than that of Schlemm's canal R_{SC}. For example, an arcuate member can have a radius of curvature of about 3 mm to about 8 mm. In some variations, the radius of curvature of an arcuate member R_{supp} in a support is about 3 mm, or about 4 mm, or about 5 mm. In other variations, the radius of curvature R_{supp} of an arcuate member in a support is about 6 mm, or about 7 mm, or about 8 mm.

The supports described here occupy at least a portion of a central core of Schlemm's canal. The central core of Schlemm's canal is the region around the cross-sectional center of the canal in the interior space of the canal lumen. A support that occupies at least a portion of the central core of the canal can traverse at least a portion of the canal lumen. For example, some variations of supports can traverse the cross-sectional center of the canal at at least one point. Referring to FIG. **12**A, a front view of a support **220** having beads **222** connected with connectors **224** is provided. FIG. **12**B shows an expanded cross-sectional view along line II-II'. Support **220** occupies a portion canal central core **67** in canal lumen **64**. Trabecular meshwork **28** is shown adjacent to canal **30**. In this variation, support **220** traverses the cross-sectional center **66** of the canal. In other variations, supports can traverse the lumen of the canal off-center, e.g., appearing as a chord across the canal lumen in cross-section. Referring to FIG. **12**C, a front view of an arcuate support **210** is shown. FIG. **12**D shows an expanded cross-sectional view along line III-III'. Support **210** traverses and occupies a portion of central core **67** in lumen **64** of canal **30** without passing through canal center **66**. In some variations, the support can occupy the majority of the central core of the canal. Referring to FIG. **12**E, a front view of support **230** comprising disc-like beads **232** is shown. A cross-sectional view along line IV-IV' is shown in FIG. **12**F. As illustrated in FIG. **12**F, bead **232** with fenestrations **234** occupies the majority of central core **67** of canal **30**. In other variations,

the support occupies only a small portion of the central core of the canal. For example, in FIG. **12**G, a front view of a support **240** having an open network structure is shown. A cross-sectional view along line V-V' is shown in FIG. **12**H.

A support can made of a variety of different materials. In general, the support should comprise a biocompatible material, such as a biocompatible polymer, ceramic or ceramic composite, glass or glass composite, metal, or combinations of these materials. Examples of biocompatible metals include stainless steel, gold, silver, titanium, tantalum, platinum and alloys thereof, cobalt and chromium alloys, and titanium nickel alloys such as Nitinol. Examples of biocompatible polymers include high density polyethylene, polyurethane, polycarbonate, polypropylene, polymethylmethacrylate, polybutylmethacryate, polyesters, polytetrafluoroethylene, silicone, polyvinyl alcohol, polyvinyl pyrrolidone, polyvinyl chloride, ethyl vinyl acetate, collagen, collagen derivatives, flexible fused silica, polyolefins, NYLON® polymer, polyimide, polyacrylamide, fluorinated elastomers, and copolymers and blends thereof. In addition, biocompatible hydrogels can be used in supports and devices described herein. As discussed in more detail below, biocompatible polymers may be biodegradable. A support can be made of a single material or a combination of materials. In some variations, a support made from a first material is coated with a second material, e.g., to enhance or improve its biocompatibility.

In some examples, the biocompatible polymer in a support will include a biodegradable polymer. Examples of suitable biodegradable polymers include collagen, a collagen derivative, a poly(lactide), a poly(glycolide), a poly(lactide-co-glycolide), a poly(lactic acid), a poly(glycolic acid), a poly(lactic acid-co-glycolic acid), a poly(lactide)/poly(ethylene glycol) copolymer, a poly(glycolide)/poly(ethylene glycol) copolymer, a poly(lactide-co-glycolide)/polyethylene glycol) copolymer, a poly(lactic acid)/poly(ethylene glycol) copolymer, a poly(glycolic acid)/poly(ethylene glycol) copolymer, a poly(lactic acid-co-glycolic acid)/poly(ethylene glycol) copolymer, a poly(caprolactone), a poly(caprolactone)poly(ethylene glycol) copolymer, a polyorthoester, a poly(phosphazene), a poly(hydroxybutyrate) or a copolymer including a poly(hdroxybutyrate), a poly(lactide-co-caprolactone), a polycarbonate, a poly(esteramide), a polyanydride, a poly(dioxanone), a poly(alykylene alkylate), a copolymer of polyethylene glycol and a polyorthoester, a biodegradable polyurethane, a poly(amino acid), a polyetherester, a polyacetal, a polycyanoacrylate, a poly(oxyethylene)/poly(oxypropylene) copolymer, and blends and copolymers thereof.

At least a portion of the support can be made from a shape memory material. For example, shape memory alloys, e.g. a nickel-titanium alloy can be used. In addition, shape memory polymers, e.g., polymers made from copolymerizing monomers oligo(e-caprolactone) dimethacrylate and n-butyl acrylate or polymers based on styrene acrylate, cyanate ester and epoxies, can be used. If a shape memory material is used in the support, the support can have a compressed state prior to and during implantation, and an expanded state following implantation. The use of a compressed state support comprising a shape memory material can allow for a smaller incision and facilitate insertion into a narrowed or compressed Schlemm's canal. Once implanted, the support can be expanding using any suitable method, e.g., thermally activated by body heat or an alternate heat source, to adopt an expanded state, thereby opening the canal.

The support can include an active agent, such as a pharmaceutical. Active agents can include prostaglandins, prostaglandin analogs, beta blockers, alpha-2 agonists, calcium channel blockers, carbonic anhydrase inhibitors, growth factors, such as tissue growth factors and vascular endothelial growth factors, anti-metabolites, chemotherapeutic agents such as mitomycin-C,5-fluorouracil, steroids, antagonists of growth factors such as antagonists of vascular endothelial growth factors, or combinations thereof. The active agent can be provided as a coating on at least a portion of a support. The active agent can be delivered throughout the eye by dissolution or other dispersal mechanisms. Alternatively, at least a portion of the support can be impregnated with the active agent. In other embodiments, the active agent can be dispersed within at least a portion of the support. For example, a cavity in the support can be filled with the active agent.

The delivery of the active agent can be controlled by time-release. For example, the portion of the support containing the active agent can include a time release coating or time release formulation designed to gradually dissipate the active agent over a certain period of time. Biodegradable coatings and formulations for time-release of active agents are known in the art. In some variations, the support can comprise multiple layers, where the layers each comprise an active agent. For example, support layers can be used to release a series of different agents, or a series of doses of the same agent. Such layers can be part of a coating applied to a support, or part of a support body. In addition, the support can comprise biodegradable layers containing no active agent that can be applied or interspersed between other layers to further control delivery of active agents to the eye.

In some variations, it will be desirable to change or alter the support using electromagnetic radiation. For example, at least a portion of a support can be fenestrated, perforated, bent, shaped or formed using a laser to enhance intraocular pressure reduction. As illustrated in FIG. **13**, predetermined localized portions **120** of support **122** can be designed to absorb light of a certain wavelength or wavelength range. Preferential absorption can be achieved by material selection and/or by doping with chromophores. Upon irradiation with sufficient energy at the selected wavelength or wavelength range, the patterned regions **120** will ablate or melt, leaving new or enlarged perforations or indentations in the support. For example, a pulsed titanium sapphire laser operating between about 750 and about 800 nm can be used to ablate gold regions. If beads **126** in support **120** are hollow, then after irradiation and ablation, features **120** will become fenestrations. The fenestrations can be created to make support **122** more porous in nature or to allow release of an active agent from within a support, e.g., from within beads **126**. Alternatively, it is possible to use a mask in combination with electromagnetic radiation to alter a support, such as by patterning or machining. The modification of a support using electromagnetic radiation can be carried out prior to or subsequent to insertion.

In some variations, the visual appearance of the support can be enhanced under certain conditions to facilitate placement or to monitor the position or condition of the support. Visual enhancement can be achieved by incorporating into or onto the support chromophores that fluoresce or phosphoresce upon excitation with a light source. Chromophores can also assist a clinician in verifying the position of the support postoperatively using a gonioscope, for example. Light sources can include lasers, lamps, and light emitting diodes. In some instances, transmission or absorption filters may be used to select the wavelength of the excitation source

or to detect or view emission. Emission from a support capable of visual enhancement may be in the wavelength range of about 300 nm to about 800 nm. The chromophores can be an integral component of the material making up the support, doped into support material, or coated or sprayed onto the support. Visually-enhancing chromophores can be applied on a temporary basis, or on a permanent basis. An example of a suitable chromophore is fluorescein, which can be excited with any laser or lamp emitting at about 400 to about 500 nm. In addition, phosphorus-based chemiluminescent or photoluminscent pigments can be used, which can be selected to absorb at various wavelengths across the visible spectrum.

In some variations, the support may be capable of being attached to tissue. For example, the support may include a hook, loop, clip, extension, or the like that may be easily attached to tissue. The support may also be attached to tissue using sutures or adhesives. The support may be attached to tissue using more than one attachment method, e.g., suturing may be used in combination with a loop, or an adhesive may be used in combination with a hook. In other variations, the support may be allowed to self-position in Schlemm's canal. In still other variations, the support may be mobile within Schlemm's canal.

Kits

Kits for reducing intraocular pressure are provided, where the kits contain at least one support that can be implanted circumferentially within Schlemm's canal configured to maintain the patency of at least a portion of Schlemm's canal. The support occupies at least a portion of a central core of Schlemm's canal and does not substantially interfere with transmural flow across the canal. The kits also provide an introducer or delivery device for implanting the support in the canal. The support and introducer are provided in packaged combination in the kits. The kits can also include instructions for use, e.g., for implanting and inspecting the support.

The introducer can be inserted into the eye and is capable of implanting the support at the desired implantation position within Schlemm's canal. For example, an introducer may include a tubular cannula through which the support may be passed. In addition to a cannula, the introducer may include a tubular or solid pusher rod that can be used to push or advance the support into and/or around Schlemm's canal. Alternatively, a pusher rod or plunger can be used without a cannula to introduce a support into the canal. A support can be installed into the lumen of a cannula prior to insertion, the distal end of the cannula positioned at or near the desired support location, and the pusher rod operated from the proximal end to push the support distally out of the distal end of the cannula and into the canal. The cannula and/or the pusher rod may be flexible and small enough in diameter to extend at least partially around the canal. In some variations, a proximal end of a suture can be introduced into the canal via a cannula and the suture extended circumferentially around the canal. A distal portion of the suture can be connected to the support and force applied to the proximal end of the suture to pull the support into the canal. The support can then be positioned within the canal by pulling the suture in a distal or proximal direction. The suture can be used to anchor the support within the canal. In other variations, the support can be directly introduced into the canal using surgical forceps, or the like.

FIGS. **14**A-D illustrate additional variations for introducing a support into the canal. As shown in FIG. **14**A, a support **200** can be introduced into the canal using syringe **202** and plunger **204**. Syringe **202** has distal end **206** that can be at least partially inserted into or placed adjacent to an opening in the canal. Force in a distal direction is applied to plunger **204**, thereby pushing support **200** into the canal. Referring to FIGS. **14**B-C, distal end **208** of guide element **210** can be at least partially introduced into the canal. Guide element **210** can be a guide wire. Guide element **210** can be extended circumferentially along the canal to aid in positioning the support. Support **212** comprises central bore **218** capable of accommodating guide element **210** such that support **212** can be threaded onto guide element **210** and slidably positioned along the guide element. Once distal end **209** of support **212** is threaded onto guide element **210**, support **212** can be pushed in a distal direction along guide element **210** to insert support **212** into the canal. In some variations, support **212** can remain threaded onto guide element **210**, and guide element **210** can remain in the canal. In other variations, support **212** can be slid off distal end **208** of guide element **210**, and the guide element can be pulled in a proximal direction for removal. Referring to FIGS. **14**C-D, syringe **202** with plunger **204** can be used in combination with a guide element **210**. In this variation, distal end **208** of guide element **210** is inserted at least partially into Schlemm's canal. Guide element **210** can be extended circumferentially along the canal to aid in positioning the support. Support **212** has central bore **218** capable of accommodating guide element **210**. Proximal end **211** of guide element **210** is inserted into bore **218**. Plunger **204** is depressed in a distal direction to push support **212** into the canal and slide support **212** along element **210**. Guide element **210** can remain in the canal or be removed following insertion of the support. Supports **200**, **212** must be sufficiently resilient to withstand force encountered as they are pushed into the canal.

In some variations, a positioning device may be used with the introducer to position or adjust the support within the canal. A positioning device can include a rod, grippers, a clamp, a hook, or the like. In other variations, a device or system capable of dilating the canal to facilitate insertion of a support may be included in the kits, e.g., a syringe or other device capable of injecting fluid into the canal.

In some variations, the kits contain at least two supports. Multiple supports can be implanted within one eye or within multiple eyes. If the kits contain multiple supports, the kits may also contain multiple introducers. Alternatively, the same introducer may be used for implantation of multiple supports, especially if the multiple supports are being delivered to a single eye. If multiple supports are to be delivered with the same introducer, then the multiple supports can be preloaded into the introducer for sterility. If more than one support is included in a kit, the supports may be of different shapes, sizes, lengths, or materials. If the kits contain more than one support to be implanted into a single eye, the supports can be connected together.

The kits can comprise an active agent, such as a pharmaceutical agent. The active agent may be included as an integral part of the support, or may be supplied in kits for application to the support or to the eye during or after implantation. Examples of active agents that may be supplied as part of the kits include prostaglandins, prostaglandin analogs, beta blockers, alpha-2 agonists, calcium channel blockers, carbonic anhydrase inhibitors, growth factors, such as tissue growth factors or vascular endothelial growth factors, anti-metabolites, chemotherapeutic agents such as mitomycin-C,5-fluorouracil, steroids, antagonists of growth factors, such as antagonists of vascular endothelial growth factor, and combinations thereof.

The kits may contain a fixation device for attaching a support to tissue. Such a fixation device can include sutures, hooks, barbs, clips, adhesives, and combinations thereof. In addition, the kits may include a system for visually enhancing the support to facilitate viewing, positioning, and monitoring of a support. A system for visually enhancing the support can include a light source, a transmission or absorption filter, a mirror, a composition comprising a chromophore capable of fluorescing or phosphorescing that can be applied to the support, or any combination thereof. Chromophores can assist a clinician in verifying the position of the support postoperatively using a gonioscope, for example. The light source is capable of exciting a chromophore contained within or on the support such that the chromophore emits fluorescence or phosphorescence. The emission is preferably within the wavelength range of about 300 nm to about 800 nm. A suitable light source for such a system can comprise a laser, a light emitting diode, or a lamp. In some instances, transmission or absorption filters may be used to further select the wavelength range of the excitation source or view or detect emission from chromophores. One or more mirrors may be used to direct a light source or emitted light, or to view the support.

Methods

Methods for reducing intraocular pressure are also provided. In general, the methods comprise inserting a support circumferentially within Schlemm's canal, such that the support maintains the patency of at least a portion of the canal. The support occupies at least a portion of a central core of Schlemm's canal and does not substantially interfere with transmural flow across Schlemm's canal.

The methods can comprise inserting a support circumferentially into Schlemm's canal using an introducer and/or a positioning device. The introducer can include a cannula and a tubular or hollow pusher rod. The support can be installed in the lumen of the cannula at its distal end and the pusher rod can be inserted into the lumen of the cannula at its proximal end and extended distally to push the support into position in the canal. In some instances, the cannula and/or the pusher rod may be flexible and small enough in diameter to at least partially extend circumferentially around the canal. In some variations of the methods, a positioning device can be used in addition to an introducer. The positioning device can comprise a second rod, a gripper, a hook, a clamp, or the like. In some variations, the methods include illuminating a support with a light source to causes the support to fluoresce or phosphoresce, thus aiding the visual appearance of the support. The illuminating of the support can occur during or after implantation to inspect the support, e.g., to monitor its position, condition, or performance.

In some instances, the methods will also comprise dilating Schlemm's canal prior to insertion of the support. Dilation of the canal can be accomplished by injecting fluid into the canal. For example, a high viscosity fluid such as sodium hyaluronate, or other dilating fluids known in the art, can be used to dilate the canal.

The methods may include implanting more than one support into an eye. In some variations, the methods will include implantation of two or more supports circumferentially adjacent to each other within the canal, and in other variations, the methods will include implantation of supports circumferentially opposed to each other within the canal, e.g., two supports centered about 180° apart around the circumference of Schlemm's canal. Some variations of the methods can comprise connecting together multiple supports in a single eye.

In some variations, the methods can include anchoring the support to tissue surrounding Schlemm's canal. Anchoring the support to tissue can be accomplished in a variety of ways, e.g., by suturing, application of adhesives, installation of hooks, clips, or the like, or combinations thereof. In other variations, the methods can comprise selecting the size of the support such that the support fits securely into the canal by a friction fit. Examples of arcuate supports that can be implanted with a friction fit are illustrated in FIGS. **11**A-C.

The methods described here can also include altering the support using electromagnetic radiation. For example, a support can include regions capable of preferentially absorbing a certain wavelength range. When electromagnetic radiation of the appropriate wavelength range with sufficient energy is incident upon the support, material in the preferentially absorbing regions will melt or ablate, resulting in perforations or indentations in the support at those regions. For example, a pulsed titanium sapphire laser emitting at about 750 nm to about 800 nm incident on gold can cause the gold to melt or ablate. The alteration of the support using electromagnetic radiation can occur before or after implantation of a support. For example, fenestrations can be created or enlarged in a support after the support has remained in an eye for a period of time to enhance drainage.

While the inventive devices, kits and methods have been described in some detail by way of illustration, such illustration is for purposes of clarity of understanding only. It will be readily apparent to those of ordinary skill in the art in light of the teachings herein that certain changes and modifications may be made thereto without departing from the spirit and scope of the appended claims. For example, it is envisioned that the devices, kits and methods can be applied to nonhuman eyes to reduce intraocular pressure, e.g., in dogs, cats, primates, or horses.

The invention claimed is:

1. A method for treating an eye condition, comprising:
implanting a support within Schlemm's canal, wherein the support comprises an arcuate member, wherein at least a portion of the arcuate member has a radius of curvature smaller than the radius of curvature of Schlemm's canal such that at least a portion of the arcuate member extends out of Schlemm's canal.

2. The method of claim **1**, wherein the support has at least one fenestration.

3. The method of claim **1**, wherein the support has a length equal to about a quarter or less than a quarter of the circumference of Schlemm's canal.

4. The method of claim **1**, wherein at least a portion of the support is made from a biocompatible polymer.

5. The method of claim **4**, wherein the biocompatible polymer comprises a biodegradable polymer.

6. The method of claim **1**, wherein at least a portion of the support is made from a shape memory material.

7. The method of claim **6**, wherein the shape memory material comprises a shape memory alloy.

8. The method of claim **7**, wherein the shape memory alloy comprises a nickel titanium alloy.

9. The method of claim **1**, wherein at least a portion of the support is made from a biocompatible metal.

10. The method of claim **9**, wherein the metal is titanium.

11. The method of claim **1**, wherein at least a portion of the support is hollow.

12. The method of claim **1**, wherein at least a portion of the support is porous.

13. The method of claim **1**, wherein when the support is disposed within a cylindrical section of the lumen of

Schlemm's canal having an internal wall surface area C, the support contacts less than 30% of C.

14. The method of claim **1**, wherein when the support is disposed within a cylindrical section of the lumen of Schlemm's canal having an internal wall surface area C, the support contacts less than 10% of C.

15. The method of claim **1**, wherein the support is flexible.

16. The method of claim **1**, wherein the support is rigid.

17. The method of claim **1**, wherein the support does not substantially interfere with longitudinal flow along Schlemm's canal.

18. The method of claim **1**, wherein the support does not substantially interfere with transmural flow into and out of Schlemm's canal.

19. The method of claim **1**, further comprising preloading the support into an introducer and delivering the support from the introducer into Schlemm's canal.

20. The method of claim **19**, wherein the support is delivered from the introducer using a pusher.

* * * * *

EXHIBIT 5

US011389328B2

(12) **United States Patent**
Badawi et al.

(10) **Patent No.: US 11,389,328 B2**
(45) **Date of Patent: *Jul. 19, 2022**

(54) **INTRAOCULAR IMPLANTS AND METHODS AND KITS THEREFOR**

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(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 656 days.

This patent is subject to a terminal disclaimer.

(21) Appl. No.: **16/413,466**

(22) Filed: **May 15, 2019**

(65) **Prior Publication Data**

US 2020/0038243 A1 Feb. 6, 2020

Related U.S. Application Data

(60) Continuation of application No. 15/182,165, filed on Jun. 14, 2016, now Pat. No. 10,314,742, which is a (Continued)

(51) **Int. Cl.**
A61F 9/007 (2006.01)
A61F 9/00 (2006.01)

(52) **U.S. Cl.**
CPC ..... ***A61F 9/00781*** (2013.01); ***A61F 9/0017*** (2013.01); *A61F 2210/0004* (2013.01); (Continued)

(58) **Field of Classification Search**
CPC A61F 9/00781; A61F 2210/0014; A61F 2250/0067
(Continued)

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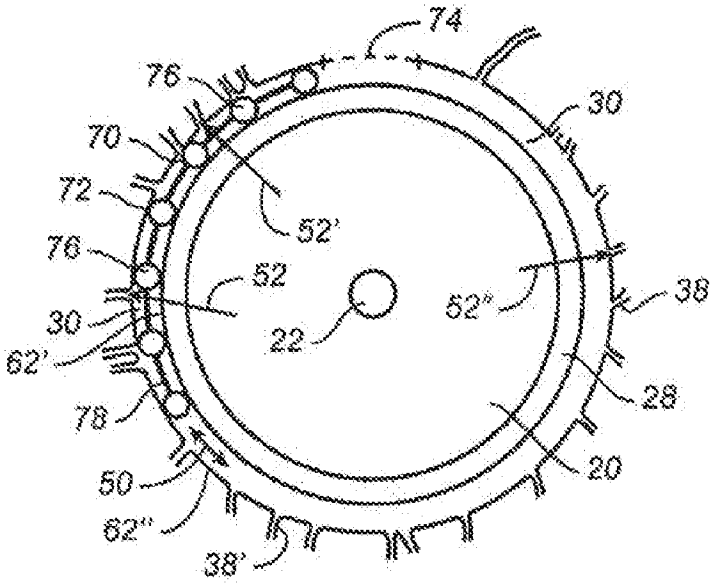
(57) **ABSTRACT**

Devices, methods and kits are described for reducing intraocular pressure. The devices include a support that is implantable within Schlemm's canal and maintains the patency of the canal without substantially interfering with transmural fluid flow across the canal. The devices utilize the natural drainage process of the eye and can be implanted with minimal trauma to the eye. Kits include a support and an introducer for implanting the support within Schlemm's canal. Methods include implanting a support within Schlemm's canal, wherein the support is capable of maintaining the patency of the canal without substantial interference with transmural fluid flow across the canal.

27 Claims, 16 Drawing Sheets



Related U.S. Application Data

continuation of application No. 13/025,112, filed on Feb. 10, 2011, now Pat. No. 9,370,443, which is a division of application No. 11/475,523, filed on Jun. 26, 2006, now Pat. No. 7,909,789.

(52) **U.S. Cl.**
CPC *A61F 2210/0014* (2013.01); *A61F 2250/0067* (2013.01)

(58) **Field of Classification Search**
USPC 604/8, 9, 264; 623/23.64, 23.7
See application file for complete search history.

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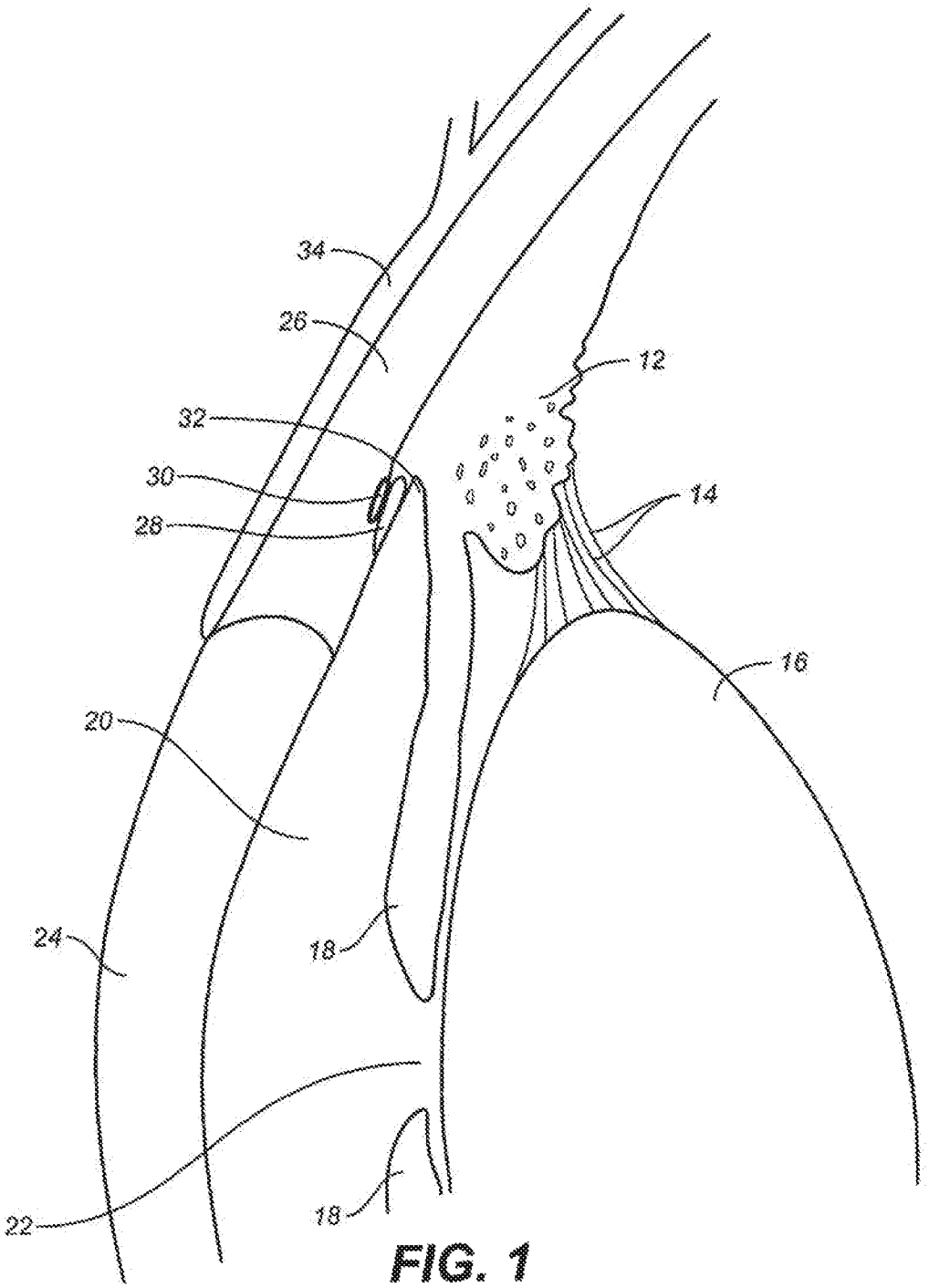


FIG. 1

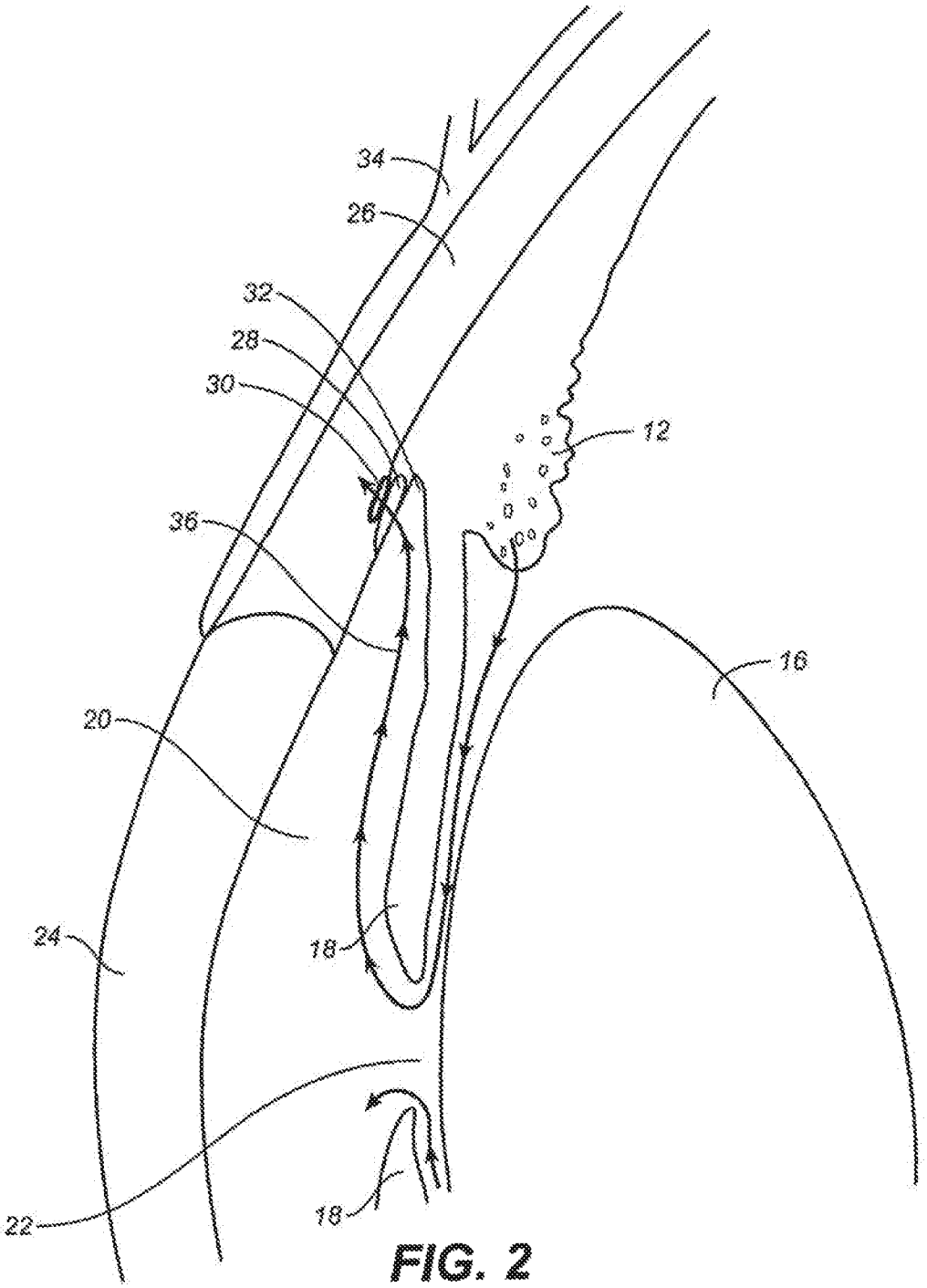


FIG. 2

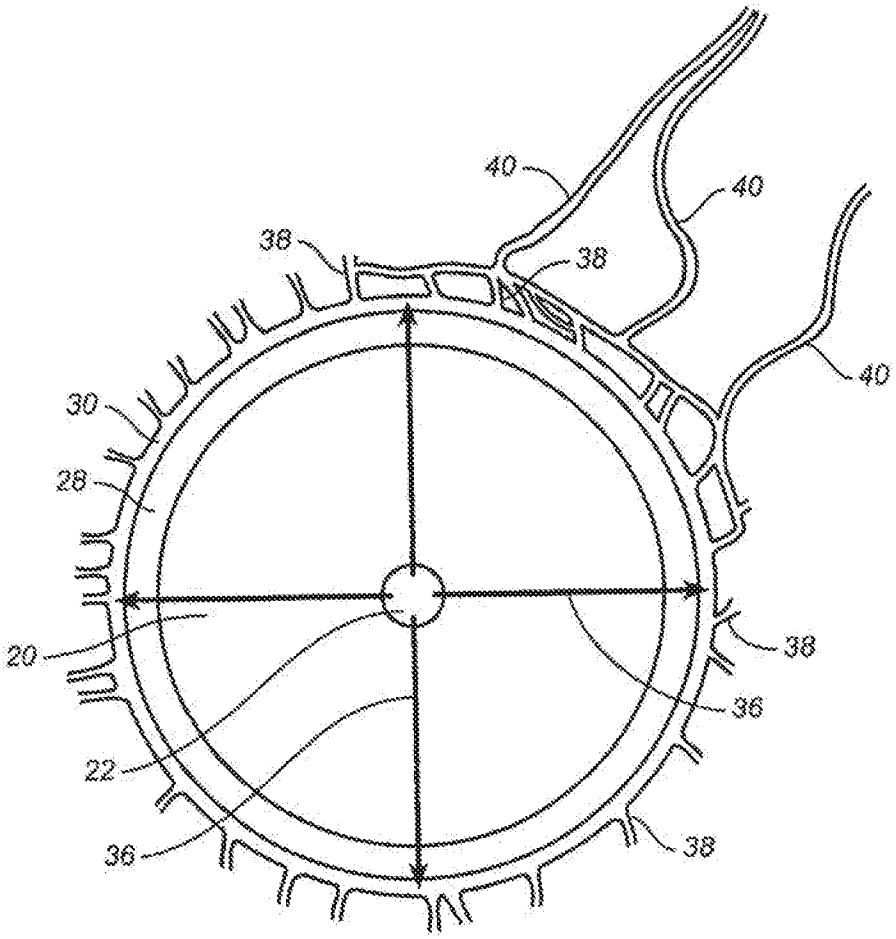
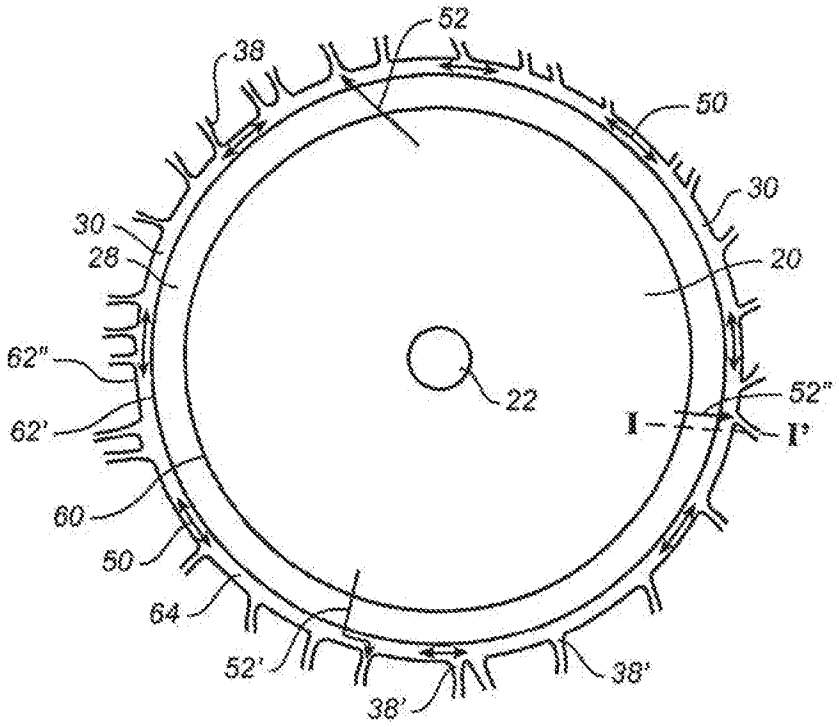


FIG. 3


52
38
50
30
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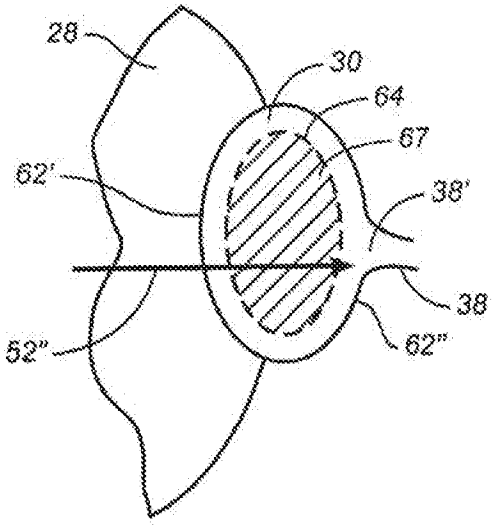
28
20
62"
22
52"
62'
I
I'
60
50
64
52'
38'
38'

FIG. 4A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64
67
62'
38'
38
52"
62"

FIG. 4B

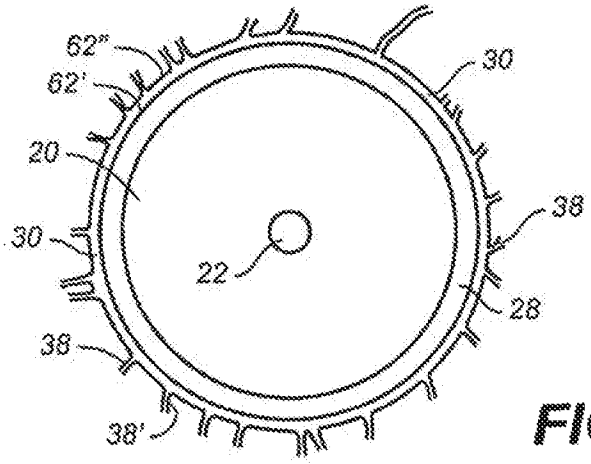


FIG. 5A

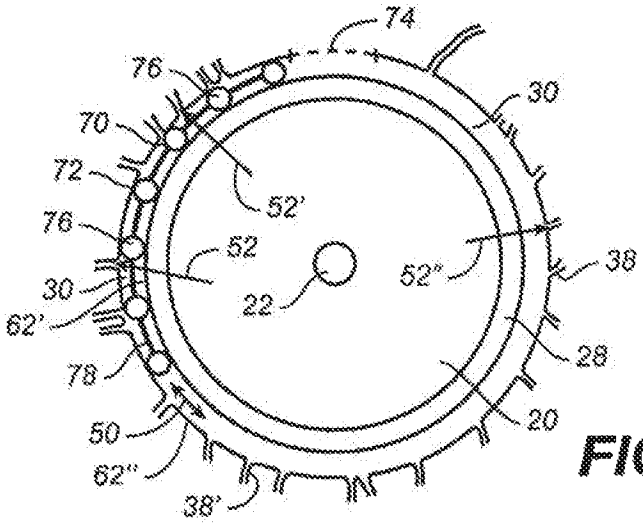


FIG. 5B

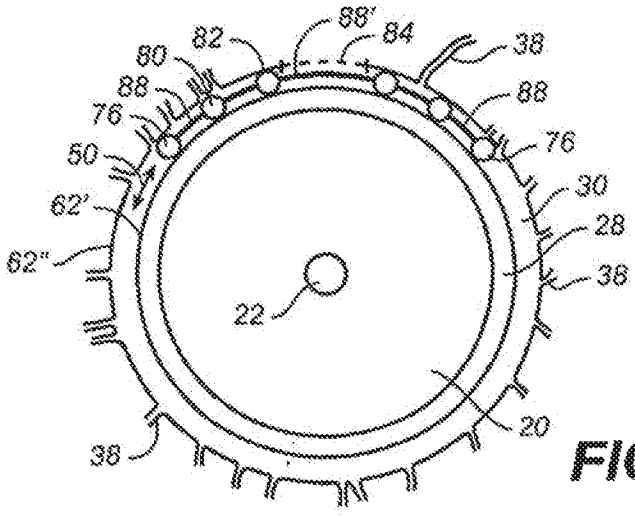


FIG. 5C

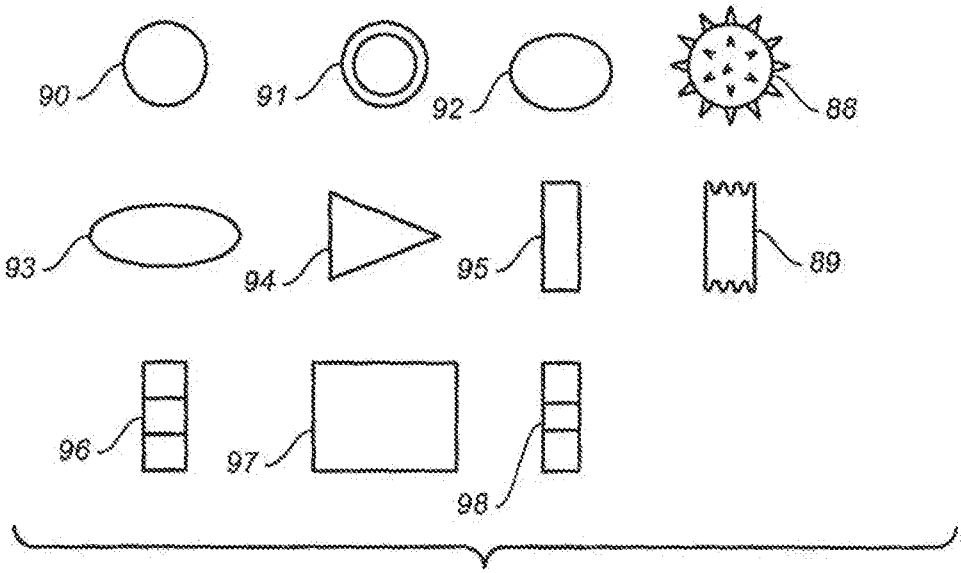


FIG. 6A

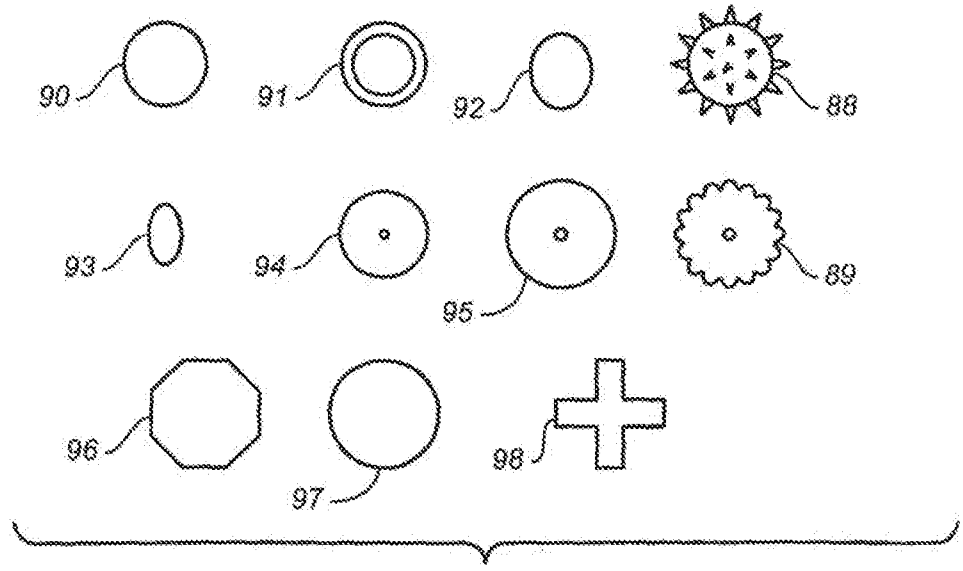


FIG. 6B

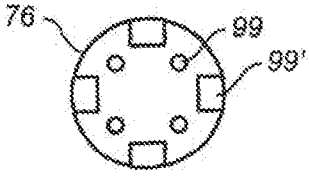


FIG. 6C

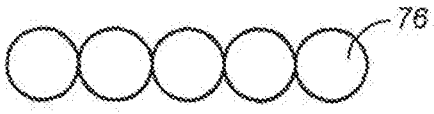


FIG. 7A

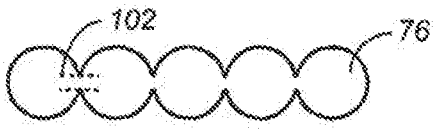


FIG. 7B

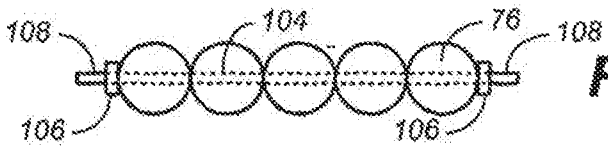


FIG. 7C

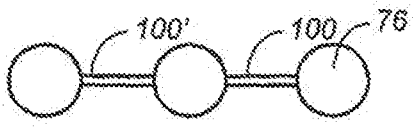


FIG. 7D

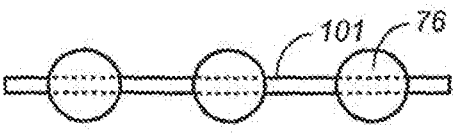


FIG. 7E

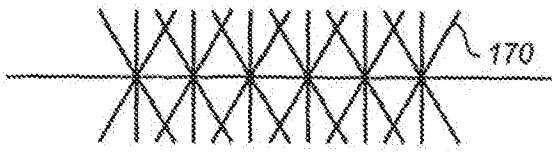


FIG. 8A

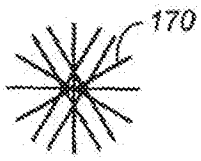


FIG. 8B

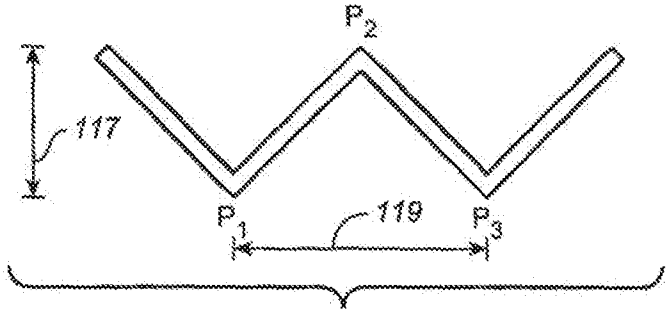


FIG. 8C

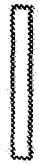


FIG. 8D

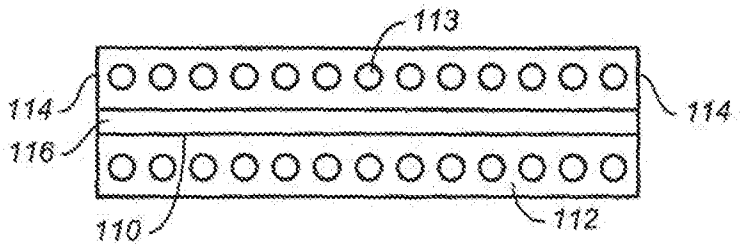


FIG. 8E

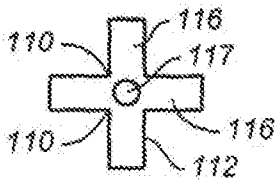


FIG. 8F

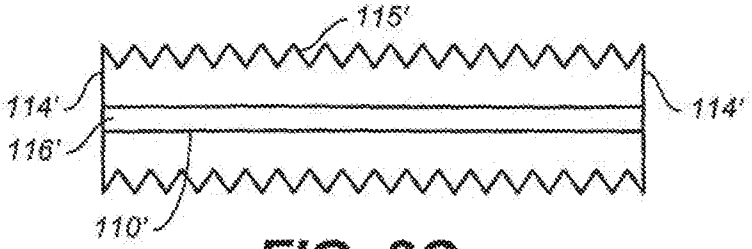


FIG. 8G

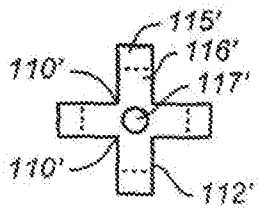
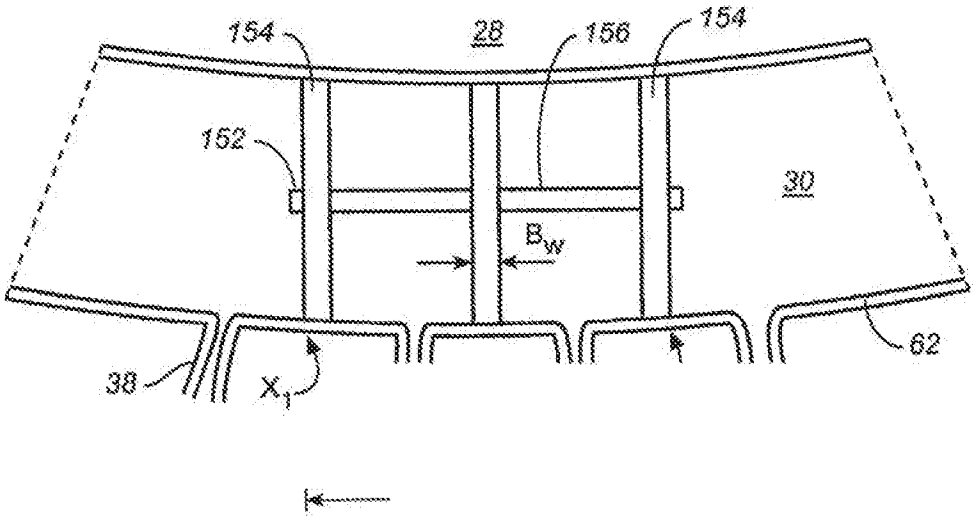


FIG. 8H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156
154
152
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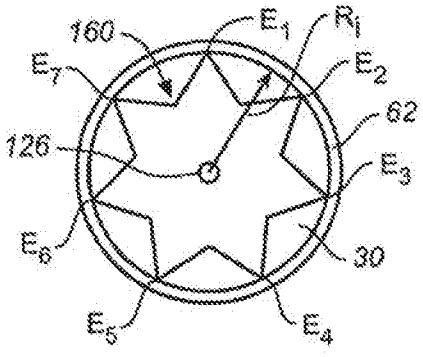
B_W
38
X_1
62

FIG. 9A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E_1
R_1
E_7
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E_5
E_4

FIG. 9B

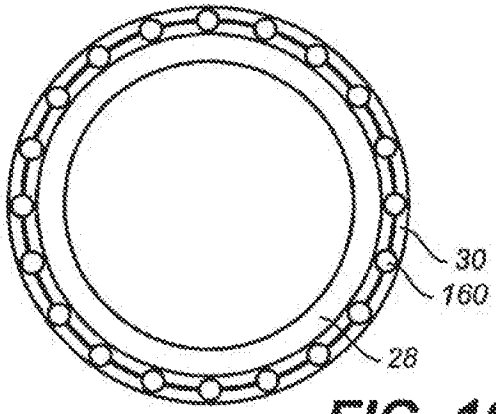


FIG. 10A

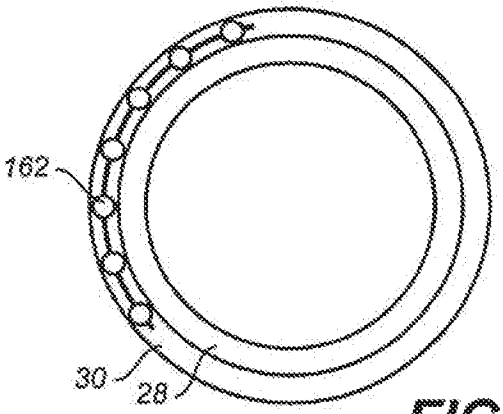


FIG. 10B

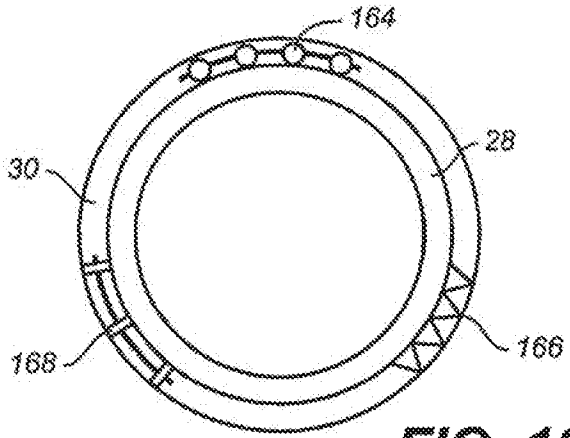


FIG. 10C

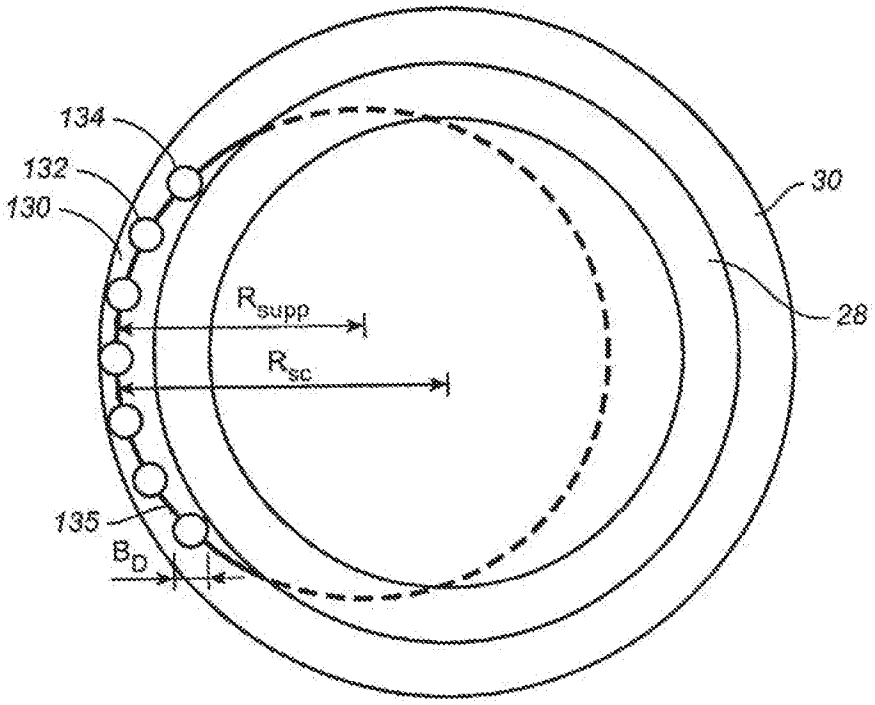


FIG. 11A

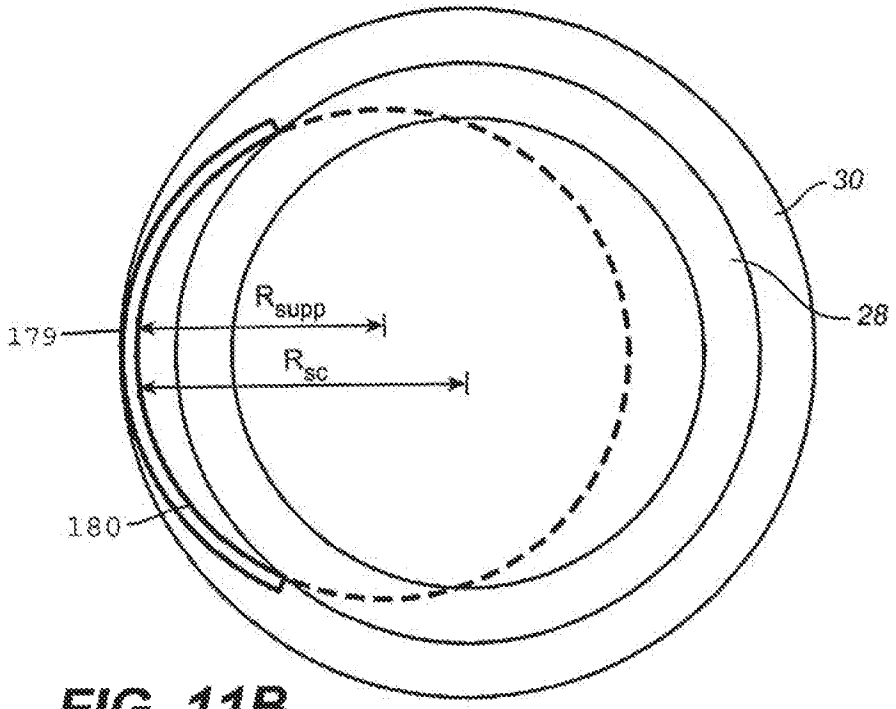
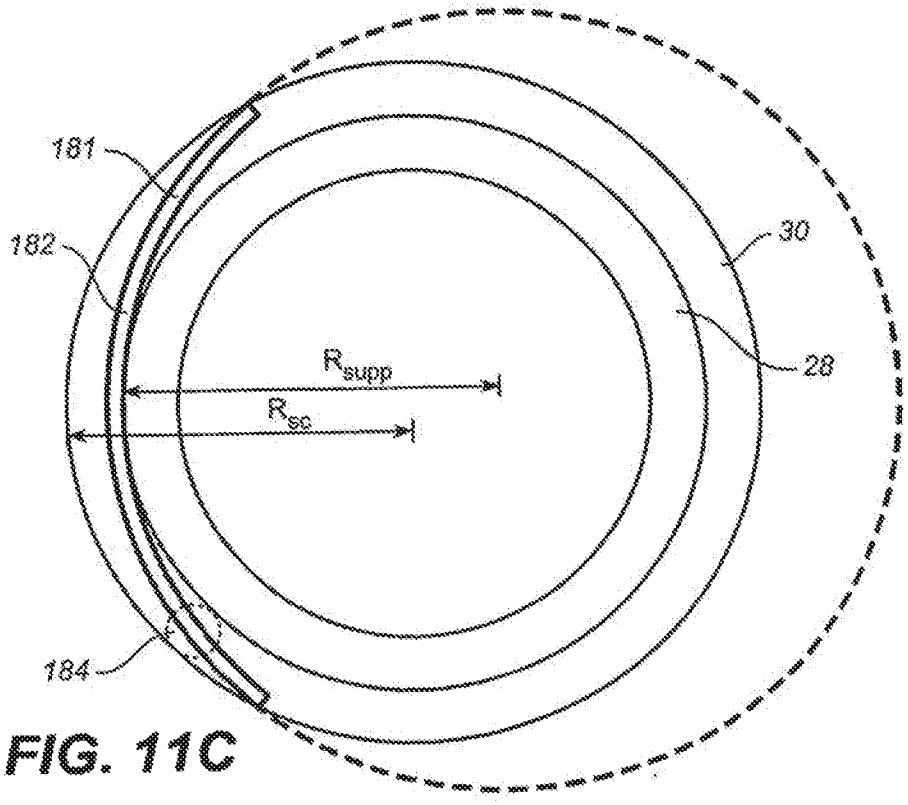


FIG. 11B



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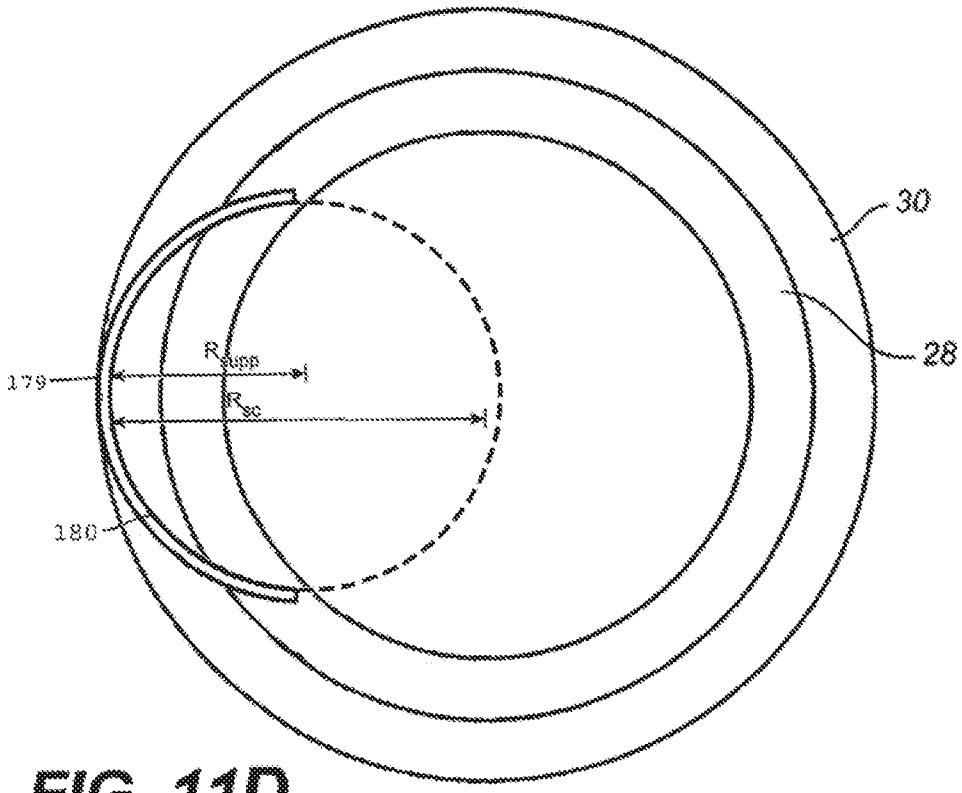

FIG. 11D

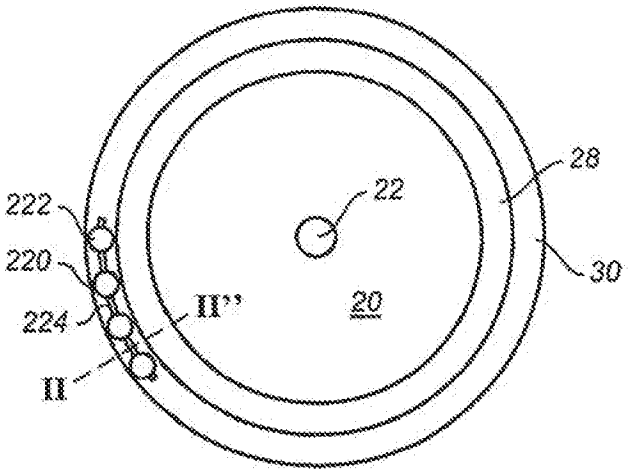

FIG. 12A

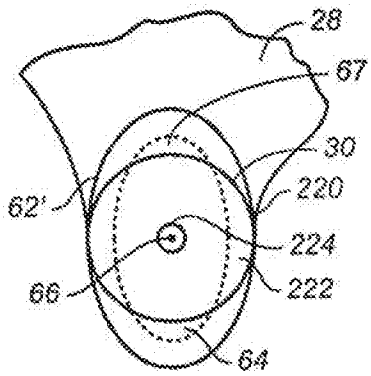

FIG. 12B

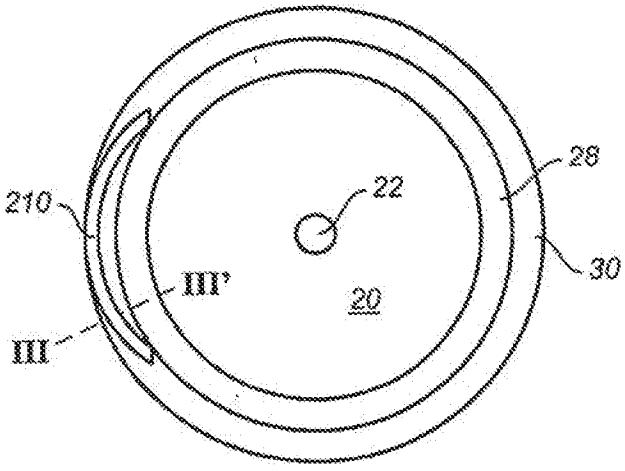

FIG. 12C

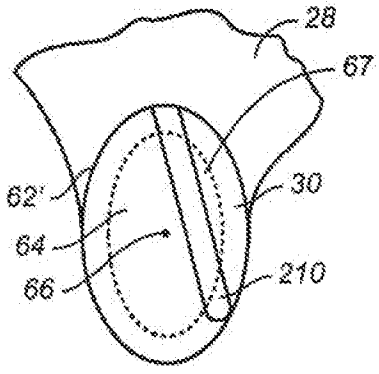

FIG. 12D

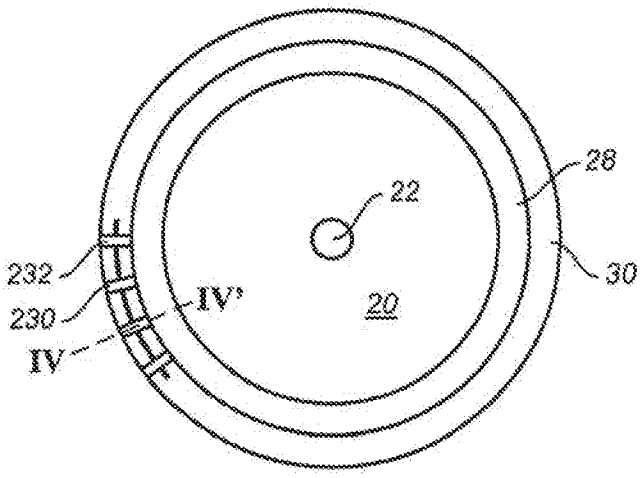

FIG. 12E

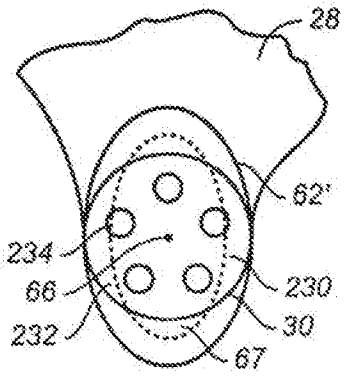

FIG. 12F

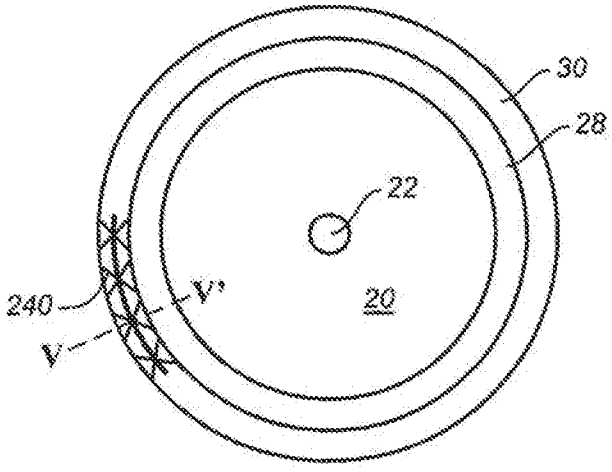

FIG. 12G

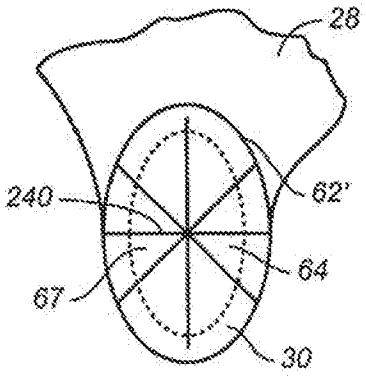

FIG. 12H

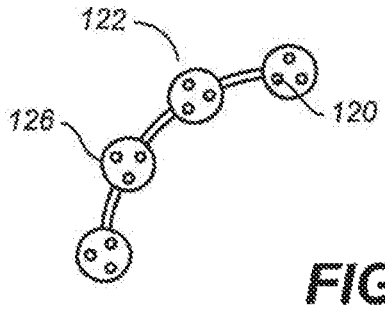

FIG. 13

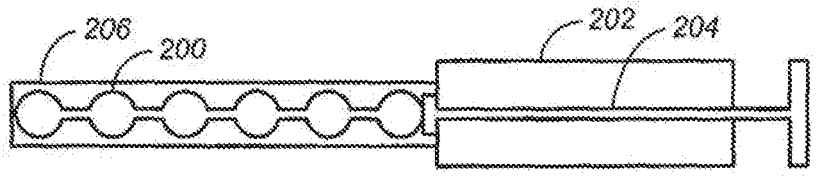

FIG. 14A

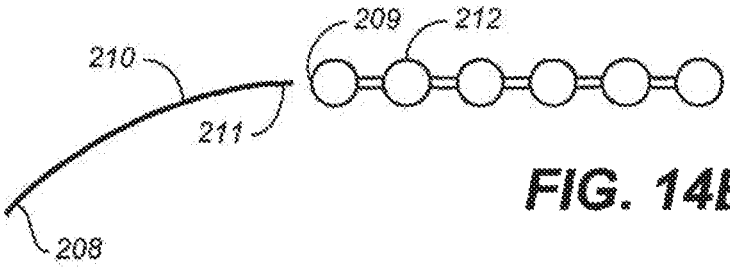

FIG. 14B

FIG. 14C

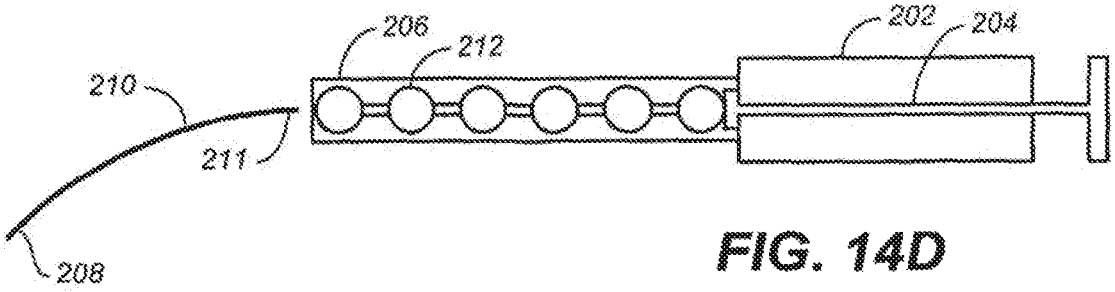

FIG. 14D

INTRAOCULAR IMPLANTS AND METHODS AND KITS THEREFOR

CROSS-REFERENCE TO RELATED APPLICATIONS

This application is a continuation of U.S. patent application Ser. No. 15/182,165, filed Jun. 14, 2016, now issued as U.S. Pat. No. 10,314,742, which is a continuation of U.S. patent application Ser. No. 13/025,112, filed Feb. 10, 2011, now issued as U.S. Pat. No. 9,370,443, which is a divisional of U.S. patent application Ser. No. 11/475,523, filed Jun. 26, 2006, now issued as U.S. Pat. No. 7,909,789, each of which is hereby incorporated by reference in its entirety.

FIELD

The devices, kits and methods described herein relate generally to intraocular pressure reduction. More particularly, the devices, kits and methods relate to intraocular implants implantable into Schlemm's canal that can reduce intraocular pressure without substantially interfering with fluid flow across Schlemm's canal.

BACKGROUND

Glaucoma is a potentially blinding disease that affects over 60 million people worldwide, or about 1-2% of the population. Typically, glaucoma is characterized by elevated intraocular pressure. Increased pressure in the eye can cause damage to the optic nerve which can lead to loss of vision if left untreated. Consistent reduction of intraocular pressure can slow down or stop progressive loss of vision associated with glaucoma. In addition, patients are often diagnosed with pre-glaucoma and ocular hypertension when they exhibit symptoms likely to lead to glaucoma, such as somewhat elevated intraocular pressure, but do not yet show indications of optic nerve damage. Treatments for glaucoma, pre-glaucoma and ocular hypertension primarily seek to reduce intraocular pressure.

Increased intraocular pressure is caused by sub-optimal efflux or drainage of fluid (aqueous humor) from the eye. Aqueous humor or fluid is a clear, colorless fluid that is continuously replenished in the eye. Aqueous humor is produced by the ciliary body, and then flows out primarily through the eye's trabecular meshwork. The trabecular meshwork extends circumferentially around the eye at the anterior chamber angle, or drainage angle, which is formed at the intersection between the peripheral iris or iris root, the anterior sclera or scleral spur and the peripheral cornea. The trabecular meshwork feeds outwardly into Schlemm's canal, a narrow circumferential passageway generally surrounding the exterior border of the trabecular meshwork. Positioned around and radially extending from Schlemm's canal are aqueous veins or collector channels that receive drained fluid. The net drainage or efflux of aqueous humor can be reduced as a result of decreased facility of outflow, decreased outflow through the trabecular meshwork and canal of Schlemm drainage apparatus, increased episcleral venous pressure, or possibly, increased production of aqueous humor. Flow out of the eye can be restricted by blockages or constriction in the trabecular meshwork and/or Schlemm's canal.

Glaucoma, pre-glaucoma and ocular hypertension currently can be treated by reducing intraocular pressure using one or more modalities, including medication, incisional surgery, laser surgery, cryosurgery, and other forms of surgery. In the United States, medications or medical therapy are typically the first lines of therapy. If medical therapy is not sufficiently effective, more invasive surgical treatments may be used. In other countries, such as those with socialized medical systems or with nationalized health care systems, surgery may be the first line of therapy if it is considered a more cost effective treatment.

A standard incisional surgical procedure to reduce intraocular pressure is trabeculectomy, or filtration surgery. This procedure involves creating a new drainage site for aqueous humor. Instead of naturally draining through the trabecular meshwork, a new drainage pathway is created by removing a portion of sclera and trabecular meshwork at the drainage angle. This creates an opening or passage between the anterior chamber and the subconjunctival space that is drained by conjunctival blood vessels and lymphatics. The new opening may be covered with sclera and/or conjuctiva to create a new reservoir called a bleb into which aqueous humor can drain. However, trabeculectomy carries both long and short term risks. These risks include blockage of the surgically-created opening through scarring or other mechanisms, hypotony or abnormally low intraocular pressure, expulsive hemorrhage, hyphema, intraocular infection or endophthalmitis, shallow anterior chamber angle, and others. Alternatives to trabeculectomy are actively being sought.

Bypass stents are also used to bridge a blocked trabecular meshwork. Stents can be inserted between the anterior chamber of the eye and Schlemm's canal, bypassing the trabecular meshwork. However, it is difficult to consistently and reliably implant a bypass stent from the anterior chamber into Schlemm's canal. The implant procedure is challenging and stents can become clogged and lose functionality over time. Others have inserted tubular elongated cylindrical hollow stents longitudinally into Schlemm's canal. Cylindrical hollow stents can be configured to allow circumferential fluid flow around the canal. These too can lose functionality over time as a result of occlusion or scarring.

Schlemm's canal is small, approximately 190-370 microns in cross-sectional diameter, and circular. Therefore, it can be difficult or expensive to design and manufacture hollow tubular stents of appropriate dimensions for use in opening Schlemm's canal. In addition, hollow tubular stents can be prone to failure and collapse or occlusion over time, as has been shown for cardiovascular stents. Hollow tubular stents incorporating thin walls are especially prone to failure. Further, the walls of tubular stents placed lengthwise along Schlemm's canal can have significant surface area contact with the trabecular meshwork and/or the collector channels, which can result in blockage of the meshwork or collector channels, substantially interfering with transmural flow across Schlemm's canal and into the eye's collector channels.

Therefore, easily manufacturable, minimally invasive devices for effective, long-term reduction in intraocular pressure are desirable. In addition, methods and kits incorporating such devices are desirable.

SUMMARY

Described here are devices, kits and methods for reducing intraocular pressure. The devices for reducing pressure within the eye comprise a support implantable circumferentially within Schlemm's canal that is configured to maintain the patency of at least a portion of the canal. The support occupies at least a portion of a central core of Schlemm's

canal. The support does not substantially interfere with transmural flow across Schlemm's canal, and thereby utilizes the eye's natural drainage pathways. The support can be implanted into Schlemm's canal with minimal trauma to the eye.

The support generally comprises a biocompatible material. At least a portion of the support can be made from a biocompatible polymer, e.g., acrylics, silicones, polymethylmethacrylate, or a hydrogel. In addition, at least part of the support can be made from a biocompatible metal such as gold. In some variations, at least a portion of the support is made from a shape memory material. Suitable shape memory materials include shape memory polymers or shape memory alloys, such as nickel titanium alloys. If a shape memory material is used, the support can have a compressed state prior to and during implantation into Schlemm's canal, and an expanded state following implantation to open the canal.

In some variations, the support is at least partially made from a biocompatible, biodegradable polymer. The biodegradable polymer can be collagen, a collagen derivative, a poly(lactide); a poly(glycolide); a poly(lactide-co-glycolide); a poly(lactic acid); a poly(glycolic acid); a poly (lactic acid-co-glycolic acid); a poly(lactide)/poly(ethylene glycol) copolymer; a poly(glycolide)/poly(ethylene glycol) copolymer; a poly(lactide-co-glycolide)/poly(ethylene glycol) copolymer; a poly(lactic acid)/poly(ethylene glycol) copolymer, a poly(glycolic acid)/poly(ethylene glycol) copolymer; a poly(lactic acid-co-glycolic acid)/poly(ethylene glycol) copolymer, a poly(caprolactone); a poly(caprolactone)/poly(ethylene glycol) copolymer, a polyorthoester, a poly(phosphazene); a poly(hydroxybutyrate) or a copolymer including a poly(hydroxybutyrate); a poly(lactide-co-caprolactone); a polycarbonate; a poly(esteramide); a polyanhydride; a poly(dioxanone); a poly(alkylene alkylate); a copolymer of polyethylene glycol and a polyorthoester, a biodegradable polyurethane; a poly(amino acid); a polyetherester; a polyacetal; a polycyanoacrylate; a poly (oxyethylene)/poly(oxypropylene) copolymer; and blends and copolymers thereof.

The support can comprise an active agent. For example, a support can be coated or impregnated with an active agent. Alternatively, an active agent can be dispersed within the support, e.g., by filling a cavity within the support. The active agent can include a prostaglandin, a prostaglandin analog, a beta blocker, an alpha-2 agonist, a calcium channel blocker, a carbonic anhydrase inhibitor, a growth factor, an anti-metabolite, a chemotherapeutic agent, a steroid, an antagonist of a growth factor, or combinations thereof. The release of the active agent can be controlled using a time release system, e.g., by embedding or encapsulating the active agent with a time release composition.

In some variations, the support will be solid. In other variations, at least a portion of the support will be hollow or porous. The surface of the support may be smooth, rough, spiked, or fluted. In still other variations, at least part of the support will be made from mesh. The support can include at least one fenestration and one or more rod-like members.

In some variations, the support comprises at least two adjacent beads. Adjacent beads can have the same or different sizes and shapes, and can be made from the same or different materials. The bead shapes can be spherical, spheroid, ovoid, cylindrical, cuboid, cubical, conical, discoid, helical, or segments thereof. In some variations, there is a connector linking at least two adjacent beads together. If there is a connector, it can be rigid or flexible. If there is more than one connector, e.g., two connectors inserted between three beads, the connectors may be of the same or different lengths. The connectors can include the same or different material as the beads they connect. A connector can also function as a spacer configured to provide space between adjacent beads. In some variations, the support comprises at least two discs separated by, and connected with, a connector. The discs may include fenestrations. The connector may also comprise a guide wire over which a fenestrated bead can be threaded into the canal of Schlemm.

The support can extend approximately all the way around Schlemm's canal, if the support has a circumference approximately equal to the circumference of Schlemm's canal. Alternatively, the support can extend only about half way around the circumference of Schlemm's canal, or about a quarter way around the canal. In some variations, the support will extend less than a quarter circumference of Schlemm's canal. The support can be configured to contact the inner surface of the wall of Schlemm's canal at two, three or more points. In some variations, the support can be attached to tissue. The support may comprise a stiff arcuate member having a radius of curvature smaller or larger than that of Schlemm's canal.

In some variations, the support can be altered using electromagnetic radiation. For example, a laser having a wavelength absorbable by at least one localized portion of the support can be used to alter the support. In other variations, electromagnetic radiation can be used to release an active agent from the support. In still other variations, the support can be visually enhanced using fluorescence or phosphorescence emission. For example, the support can comprise a chromophore that fluoresces or phosphoresces upon excitation with a light source. In some variations, the emitted fluorescence or phosphorescence is in the wavelength range of about 300 nm to about 800 nm. In some variations, the support can comprise a chromophore that enhances postoperative monitoring of the support.

Kits for reducing intraocular pressure are also provided. The kits contain a support that can be implanted circumferentially within Schlemm's canal. The support is configured to maintain the patency of at least part of Schlemm's canal. The support occupies at least a portion of a central core of Schlemm's canal and does not substantially interfere with transmural flow across the canal. The kits also contain an introducer for implanting the support within the canal. In some variations, the kits include a positioning device for adjusting the support within the canal. In other variations, kits include instructions. In still other variations, the kits include an active agent. Some kits contain at least two supports. If more than one support is included, the kits can include at least two introducers for delivering the supports. Multiple supports within the same kit can have the same or different shape, size, or composition. Multiple supports within the same kit can be connected together or remain separate. In some variations, kits include a fixation device for attaching a support to tissue. In other variations, kits may include a system for visually enhancing the appearance of the support.

Methods for reducing intraocular pressure are also described. The methods include inserting a support circumferentially within Schlemm's canal. The support is configured to maintain the patency of at least part of the canal. The support occupies at least a portion of a central core of Schlemm's canal, and does not substantially interfere with transmural flow across the canal. In some variations, the methods also include dilating Schlemm's canal prior to insertion of the support. In still other variations, the methods comprise anchoring the support to tissue. The methods can

include implanting at least two supports. If more than one support is implanted within a single eye, the multiple supports can be positioned circumferentially adjacent to each other or circumferentially opposed (i.e., positioned about 180° apart) to each other within Schlemm's canal. Multiple supports within one eye can be connected or remain separate. In some variations of the methods, the support is illuminated with a light source to visually enhance the position of the support. In other variations of the methods, the support can be altered using electromagnetic radiation. For example, a laser absorbed by at least one localized portion of the support can be used to alter the support. The alteration can comprise the creation or enlargement of an aperture in the support. If electromagnetic radiation is used to alter a support, the alteration can occur before implantation or after implantation.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. **1** provides a partial cross-sectional side view of a normal human eye.

FIG. **2** provides a partial cross-sectional side view of a normal drainage path of fluid from the eye.

FIG. **3** shows a front view of normal fluid drainage from the eye.

FIG. **4**A shows an alternative front view of normal fluid drainage paths from the eye. FIG. **4**B shows a cross-sectional view along line I-I'.

FIG. **5**A provides a front view of an eye in which Schlemm's canal is narrowed or collapsed. FIG. **5**B shows a front view of a device including a support inserted into Schlemm's canal that allows transmural flow across the canal. FIG. **5**C illustrates an alternate design for a device inserted into Schlemm's canal that allows transmural flow across the canal.

FIG. **6**A shows side views of various element or bead configurations that can be used in the supports described herein. FIG. **6**B shows the corresponding front views of the element or bead configurations shown in FIG. **6**A. FIG. **6**C illustrates an element or bead having fenestrations.

FIG. **7**A illustrates a support having multiple juxtaposed beads. FIG. **7**B illustrates a support having multiple juxtaposed and connected beads. FIG. **7**C shows an alternate configuration of a support having multiple juxtaposed and connected beads. FIG. **7**D shows a support having multiple, spaced-apart but connected beads. FIG. **7**E illustrates beads threaded onto a connector.

FIGS. **8**A-B show side and front views, respectively, of a support having an open network structure. FIGS. **8**C-D show side and front views, respectively, of a support having a longitudinal zig-zag configuration that will contact the wall of Schlemm's canal at least three points (labeled P_1, P_2, P_3). FIGS. **8**E-F show side and front views, respectively, of a support having a rod-like member with continuously fluted edges and fenestrations. FIGS. **8**G-H show side and front views, respectively, of another variation of a support having a rod-like member with continuously fluted edges.

FIGS. **9**A-B show expanded cross-sectional views of a support implanted within Schlemm's canal.

FIGS. **10**A-C illustrate various configurations of supports implanted into Schlemm's canal.

FIGS. **11**A-B and D illustrate configurations of supports having a smaller radius of curvature then Schlemm's canal. FIG. **11**C shows a support having a larger radius of curvature than Schlemm's canal.

FIG. **12**A illustrates a variation of a support traversing the center of the central core of Schlemm's canal. FIG. **12**B shows a cross-sectional view along line II-II'. FIG. **12**C illustrates a variation of a support traversing the central core of the canal. FIG. **12**D shows a cross-sectional view along line III-III'. FIG. **12**E illustrates a variation of a support that occupies the majority of the central core of the canal. FIG. **12**F shows a cross-sectional view along line IV-IV'. FIG. **12**G illustrates a variation of support having an open network that occupies a portion of the central core of the canal. FIG. **12**H shows a cross-sectional view along line V-V'.

FIG. **13** shows an illustrative example of a support that can be modified using electromagnetic radiation.

FIG. **14**A illustrates a syringe that can be used to insert a support into Schlemm's canal. FIG. **14**B illustrates a variation in which a support is threaded onto a guide element for insertion and positioning in Schlemm's canal. FIG. **14**C illustrates a cross-sectional view of a support having a central bore to accommodate a guide element. FIG. **14**D illustrates a variation in which a syringe and a guide element are used for insertion and positioning of a support in Schlemm's canal.

DETAILED DESCRIPTION

Described here are devices, kits and methods to reduce intraocular pressure by maintaining or restoring Schlemm's canal so that at least a portion of the canal is patent or unobstructed. The devices, kits and methods operate to keep Schlemm's canal from collapsing while not substantially interfering with the eye's natural drainage mechanism for aqueous humor, in which transmural fluid flow across Schlemm's canal occurs. The devices are implantable in Schlemm's canal with minimal trauma to the eye.

With reference to the figures, FIG. **1** shows a partial cross-sectional view of the anatomy of a normal human eye. Ciliary body **12** is connected to iris **18** and to lens **16** via zonular fibrils **14**. The anterior chamber of the eye **20** is bounded on its anterior (front) surface by cornea **24**. In the center of iris **18** is pupil **22**. Cornea **24** is connected on its periphery to sclera **26**, which is a tough fibrous tissue forming the white shell of the eye. Trabecular meshwork **28** is located on the outer peripheral surface of anterior chamber **20**. The trabecular meshwork extends **3600** circumferentially around the anterior chamber. Located on the outer peripheral surface of meshwork **28** is Schlemm's canal **30**. Schlemm's canal extends **3600** circumferentially around the trabecular meshwork. At the apex formed between iris **18**, meshwork **28** and sclera **26** is angle **32**. Conjunctiva **34** is a membrane overlaying sclera **26** and lining the inside of the eyelid (not shown).

FIG. **2** shows a partial cross-sectional view of flow of aqueous humor within and out of a normally functioning human eye. Aqueous humor is produced in ciliary body **12** and its path through and out of the eye is indicated by solid directional line **36**. The aqueous humor flows from ciliary body **12**, between lens **16** and iris **18**, through pupil **22** into anterior chamber **20**, across trabecular meshwork **28**, across Schlemm's canal **30**, into aqueous veins or collector channels (not shown) and finally into the bloodstream via conjunctival vasculature.

FIG. **3** shows a front view of normal flow of aqueous humor out of the eye. Aqueous humor enters anterior chamber **20** via pupil **22**. The fluid flows outwardly toward the periphery of the eye, with the general path of flow indicated by solid directional lines **36**. The fluid crosses trabecular meshwork **28** and traverses Schlemm's canal **30** to reach aqueous veins or collector channels **38**. There are typically 25-30 collector channels located in a human eye. Collector

channels **38** are connected to vasculature **40**, whereby the drained aqueous humor enters the bloodstream. Although the direction of net or bulk fluid flow is depicted as radially outward by directional lines **36** from pupil **22** for simplicity, actual fluid flow in an eye may follow more varied paths.

Different fluid flow paths in and across Schlemm's canal are illustrated in FIGS. **4**A-B. FIG. **4**A shows a front view of an eye, and FIG. **4**B shows an expanded cross-sectional view along line I-I'. Circumferential (i.e., longitudinal) flow along and around circular canal **30** is depicted by directional lines **50**. Fluid that does not traverse canal **30** to reach collector channels **38** may not be effectively drained from the eye. Examples of fluid flow paths that can effectively drain the eye are illustrated by directional lines **52**, **52'**, and **52"**. In each of these paths, fluid enters trabecular meshwork **28** along its inner peripheral surface **60** and exits the meshwork along its outer peripheral surface **62'**. Meshwork outer peripheral surface **62'** provides the inner peripheral surface or wall of Schlemm's canal **30**. Transmural fluid flow across Schlemm's canal involves two instances of transmural flow across walls or boundaries. First, fluid must flow from trabecular meshwork **38** through inner peripheral surface or wall **62'** of Schlemm's canal **30** to reach lumen **64** of the canal. Second, fluid must flow from lumen **64** through canal outer peripheral wall **62"** through apertures **38'** to enter collector channels **38**. Finally, the collector channels **38** feed the drained fluid into vasculature. Lumen **64** of canal **30** includes a central core region **67**. Thus, fluid flow from the eye differs from fluid flow in other vessels in the body where fluid need only flow longitudinally along the vessel, such as blood flowing through a vein.

Devices

Devices to reduce intraocular pressure comprising a support that can be implanted circumferentially in Schlemm's canal to maintain the patency of at least a portion of the canal are described here. The support occupies at least a portion of a central core of Schlemm's canal and does not substantially interfere with transmural flow across the canal. By "maintain the patency" of at least a portion the canal, it is meant that the support operates to keep the canal at least partially unobstructed to transmural flow, such that fluid can 1) exit through the trabecular meshwork; 2) traverse the canal; and 3) drain via the collector channels. To maintain the patency of the canal, it is not necessary that the support leave the canal unobstructed in regard to circumferential flow. By "does not substantially interfere" with transmural flow, it is meant that the support does not significantly block either fluid outflow from the trabecular meshwork or fluid outflow to the collector channels. In many variations, the support allows between about 0.1 and about 5 microliters per minute aqueous outflux from the eye through the trabecular meshwork and collector channels. The "central core of Schlemm's canal" refers to the region around the cross-sectional center of the canal in the interior space of the canal lumen, i.e., not on the periphery of the canal. Therefore, a device that occupies at least a portion of a central core of Schlemm's canal can traverse at least a portion of the canal's lumen.

Therefore, devices described here need not comprise an open-ended tubular support placed longitudinally along Schlemm's canal, i.e., the devices and supports can be non-tubular. A longitudinal, open-ended tubular support can enable longitudinal flow along the canal. However, even if fluid can flow longitudinally (i.e., circumferentially) along Schlemm's canal, the eye may not be effectively drained unless the fluid eventually traverses the canal. That is, transmural fluid flow across two boundaries must occur: 1) fluid must flow from the trabecular meshwork through a canal inner wall coincident with an outer peripheral boundary of the trabecular meshwork to reach the canal lumen; and 2) fluid must flow from the canal lumen through apertures in the canal outer peripheral wall to reach the connector channels. The collector channels are then able to further disperse the fluid and complete the natural draining process. A tubular support inserted longitudinally into the canal can have significant surface area overlap with surfaces of the canal such that transmural flow across the canal may be significantly impeded. A longitudinal tubular support placed in Schlemm's canal may block flow into the canal from the trabecular meshwork and block flow out of the canal into the collector channels.

Devices described herein for treating elevated intraocular pressure include a support that is implanted within Schlemm's canal. In many instances, the device will reduce the intraocular pressure by 1-40 mm Hg, for example by at least 2 mm Hg. In other instances, the device will reduce intraocular pressure by at least 4 mm Hg, or at least 6 mm Hg, or at least 10 or 20 mm Hg. In still other instances, the device will operate to bring the intraocular pressure into the range of about 8 to about 22 mm Hg. The support can be configured in a variety of ways to at least partially prop open Schlemm's canal thereby maintaining its patency without substantially interfering with or impeding transmural fluid flow across Schlemm's canal. In some variations, the support may interfere with or block longitudinal flow along or around the canal. In many instances, the support will be contained entirely within Schlemm's canal. In some variations the support will be implanted within the canal, but may extend partially beyond Schlemm's canal, e.g., into the trabecular meshwork.

In some variations, a support to maintain at least partial patency for Schlemm's canal to enable fluid flow between an inner wall of the canal and an outer wall of the canal can comprise elements or structures such as bead-like elements or beads, which can be connected together, e.g., as a string of beads. Individual elements or beads or a connected group of elements or beads can be inserted directly into Schlemm's canal. A more detailed description of supports incorporating elements or beads is provided below.

FIG. **5**A illustrates a front view of an eye having a narrowed or collapsed Schlemm's canal **30**, where canal outer peripheral wall **62"** is very close to canal inner peripheral wall **62'**. Although Schlemm's canal **30** is depicted in FIG. **5**A as being uniformly narrow around the entire circumference of canal, it is possible that only a portion of Schlemm's canal is narrowed or collapsed. When Schlemm's canal is collapsed or narrowed, net efflux of aqueous from the anterior chamber to the collector channels **38** is diminished, thereby increasing intraocular pressure. As a result, the risk of pre-glaucoma, ocular hypertension, or glaucoma can increase.

FIG. **5**B illustrates an example of a device **70** inserted into Schlemm's canal **30** through incision site **74**. Device **70** in this example is positioned to one side of incision site **74**. Device **70** includes support **72** that is configured to keep Schlemm's canal at least partially open to transmural fluid flow across both canal inner wall **62'** and canal outer wall **62"** to reach collector channels **38** via apertures **38'**. In the example shown in FIG. **5**B, support **72** includes elements or beads **76** connected with connectors **78**. In this variation, the distance between canal inner wall **62'** and outer wall **62"** is approximately determined by the cross-sectional dimension of support **72**, which is in turn determined by the largest cross-sectional diameter of the beads **76**. Therefore, circum-

ferential (i.e., longitudinal) fluid flow around and along the canal **30** indicated by directional line **50** may be inhibited by the insertion of support **72** into the canal. However, transmural flow across both walls or boundaries of the canal indicated by directional lines **52**, **52'**, **52"** is enhanced by support **72** and fluid is able to reach collector channels **38** and be drained from the eye. As a result, support **72** can effectively reduce intraocular pressure by utilizing the eye's natural drainage mechanism. Incision **74** need only be large enough to accommodate the diameter of beads **76**, so that trauma to the eye is minimized. Beads can have cross-sectional dimensions in the range from about 50 microns to about 500 microns. Insertion of beads having relatively small cross-sectional diameters (e.g., about 50 microns) into Schlemm's canal open the canal less than the normal cross-sectional diameter of the canal, which is about 190 to about 370 microns, but still can maintain the patency of the canal. Insertion of beads having relatively large cross-sectional diameters (e.g., greater than about 300 microns) can open the canal as large as or larger than the canal's normal cross-sectional diameter and also can operate to stretch the trabecular meshwork. Stretching the trabecular meshwork may further enhance drainage.

FIG. **5**C illustrates an alternate configuration of a device **80** inserted into Schlemm's canal **30** through incision site **84**. Device **80** includes support **82** that extends to both sides of incision site **84**. Support **82** includes elements or beads **76** connected with connectors **88** and **88'**. In this example, connector **88'** is of a different length than connectors **88**. As in FIG. **5**B, beads **76** may impede circumferential (i.e., longitudinal) fluid flow around and along canal **30** indicated by directional line **50**. However transmural flow across the canal is enhanced by support **82** that maintains patency across the canal and allows fluid to reach collector channels **38**. If the beads are fenestrated or comprise rough, spiked, or fluted perimeters, then circumferential fluid flow through or around the beads may also occur.

Elements or beads used in a support may be hollow and closed structures, open structures, solid structures, porous structures, or any combination thereof, and may be of any suitable shape. FIGS. **6**A and **6**B illustrate side and front views, respectively, of exemplary elements or beads that may be used in the supports described here. As shown, solid **90** or hollow **91**, spherical **90**, spheroid **92**, ovoid **93**, conical **94**, disk-shaped **95**, polyhedral **96**, rod-like **97**, or beads with fluted edges **98**, rough edges. **89**, or spiked edges **88** may be used. In some instances, it may be desired to round corners or edges of the beads. As illustrated in FIG. **6**C, elements or beads **76** may include fenestrations **99**, **99'**. Fenestrations may have any suitable cross-sectional shape, such as round or quadrilateral. Although a disc-shaped bead **76** is shown in FIG. **6**C, any shape of bead can be fenestrated.

As illustrated in the variations shown in FIGS. **7**A-E, two or more beads **76** in a support may be adjacent to each other. Adjacent beads may be juxtaposed (FIG. **7**A), connected and juxtaposed (FIGS. **7**B and **7**C), or connected together with connectors **100**, **100'** to form intervals between beads (FIG. **7**D). In addition, beads may be threaded onto a connector **101** (FIG. **7**E). Multiple beads used in a single support may have the same or different shapes, and may be made of the same or different materials.

Junctions **102** between beads as shown in FIG. **7**B can be made using any suitable technique, such as by using an adhesive, chemical bonding, mechanical interlocking, or welding. Beads may also be juxtaposed and connected as shown in FIG. **7**C by threading onto a guide element **104**. Guide element **104** can comprise a fiber, a suture, a guide wire, a fixture, or the like. The beads can be fixed in a juxtaposed configuration on a guide element, e.g., by knotting ends of the fiber or by providing other end-blocking devices **106**, such as clips, caps, protrusions, or the like on ends **108** of element **104**. Any or all of the beads can be attached to guide element **104**, e.g., beads occupying end positions may be attached to element **104** and function as blocking beads to keep beads from sliding off ends **108** of element **104**. Alternatively, beads may slide along element **104**. Guide element **104** can be flexible, such as thin polymer threads, such as a suture, or metal wires. Alternatively, element **104** can be flexible but fixable, such as one or more shapeable metal wires that can be bent into a desired position and maintain that position against some amount of external stress or pressure. In other variations, guide element **104** can be rigid, e.g., a molded polymeric piece or a stiff metal piece.

As shown in FIG. **7**D, multiple connectors **100**, **100'** may be used in a single support, with at least one connector inserted between adjacent beads **76**. If multiple connectors are used, they may be of the same or different lengths. In addition, multiple connectors within the same support may be made of the same or different materials, and the connectors may be made of the same or different materials than the beads. Discrete connectors **100**, **100'** can be inserted between beads **76** and attached to adjacent beads using any suitable method including using adhesives, chemical bonding, welding, mechanical interlocking, knots, or any combination thereof. In some variations, connectors **100**, **100'** between beads can be configured to function as spacers between individual beads. As illustrated in FIG. **7**E, beads **76** can also be threaded onto a connector **101**. If the beads are threaded onto a connector, the beads can be maintained in fixed positions along the connector **101** by any suitable method, including using adhesives, chemical bonding, welding, clips, protrusions on the connector, mechanical interlocking locking between a connector and a bead, knots, or any combination thereof. Alternatively, some or all beads may slide along connector **101**. Connectors **100**, **100'**, **101** can be flexible, such as thin polymer threads or metal wires. Connectors **100**, **100'**. **101** can also be flexible but fixable, such as shapeable metal wires. Alternatively, connectors **100**, **100'**, **101** may be rigid, such as molded polymeric connectors or stiff metal connectors.

Supports of the devices described here need not contain beads. For example, a support can be a unitary structure of fixed or variable length. Supports can be solid, hollow, or porous, or any combination thereof. For example, a support can be partially solid and partially hollow. Examples of support configurations are shown in side view and front view in FIGS. **8**A-F. As illustrated in FIG. **8**A-B, a support can have an open network structure. Such a support can be fabricated out of shapeable metal wires, for example. The support illustrated in FIGS. **8**A-B will have minimal surface area contact with the walls of Schlemm's canal. i.e., only point contacts at the end of wires or fibers **170**. Alternatively, a support having an open network structure can be at least partially made from a mesh or foam. The mesh or foam can be made of any suitable material, e.g., metal or plastic. As shown in FIGS. **8**C-D, the support can have a sinusoidal or zig-zag configuration extending along a selected length of Schlemm's canal. For the example shown in FIG. **8**C, the support will contact the wall of Schlemm's canal at at least three points, labeled P_1, P_2, and P_3, after implantation. In FIGS. **8**E-H, examples of rod-like supports having fluted edges are shown. In FIGS. **8**E-F, fluted edges **110** extend longitudinally along sides **112** between ends **114** of the support to form structures **116**. Structures **116** can include

fenestrations **113**. The support can include central bore **117**. In FIGS. **8**G-H, fluted edges **110'** extend along sides **112'** to form structures **116'**. Structures **116'** have serrated outer surfaces **115'** extending between ends **114'**. The support can include central bore **117'**. In the variations illustrated in FIGS. **8**E-H, the support may contact the canal walls at at least four points. In some variations, the support is adjustable.

A common characteristic of the support configurations described here is that they need not have continuous or extensive contact with a wall of Schlemm's canal. Indeed, many of the described devices and structures have minimal tangential, periodic, or sporadic contact with the wall. The surface of the support can be rough, smooth, spiked or fluted. As the example shown in FIGS. **8**A-B shows, some supports only have point contacts with the canal wall. For the supports shown in FIGS. **5**B-C, the rounded beads of each of the supports make only tangential contact with the canal wall. Bead shapes can be selected or designed to have minimal surface area contact with canal walls, e.g., beads **98** having fluted edges as shown in FIGS. **6**A-B may have low surface area contact with canal walls. In addition, supports having widely spaced apart beads, e.g., by connectors illustrated in FIGS. **7**D-E that can function to space beads at desired intervals to reduce contact with canal walls yet operate to keep the canal open. As illustrated above with respect to FIGS. **8**C-D, in some variations, the support contacts the interior wall of the canal at at least two points; or at at least three points.

Expanded cross-sectional views of a support **152** implanted circumferentially in Schlemm's canal are provided FIGS. **9**A-B. The fraction of canal wall surface area in contact with a support can be estimated by viewing the inside of Schlemm's canal as a slightly arcuate cylinder C having length L, extending circumferentially from a first end X_1 to a second end X_2 of support **152**, and inside radius R_i. In some variations, the support contacts less than 0.1% or less than 1% of the surface area of the cylinder C as described above. In other variations, the support contacts less than 10% of the surface area of C. In still other variations, the support contacts less than 30% of the surface area of C. For example, the support **152** shown in FIGS. **9**A-B contacts the canal wall **62** only at bead outer peripheral edges at E_1-E_7, along a distance of the bead width B_W. There is no contact with the canal walls where connectors **156** space apart beads **154**, and no contact in fluted regions **160** of beads **154**. The design feature of minimal support contact with canal walls allows a support to maintain patency of the canal without substantially interfering with transmural flow across the canal. If a substantial portion of the surface area of the inner periphery of the canal adjacent to the trabecular network or of the surface area of the outer periphery of the canal where the collector channels are located is blocked, effective fluid flow across the canal may be impaired.

Supports can have variable lengths and thicknesses. For example, the length of supports using beads can be tuned by varying the number, type, or spacing of beads, or any combination thereof. The thickness of a support can be increased by adding one or more beads having larger dimensions. Unitary supports can also be built with varying lengths, or with adjustable (e.g., trimmable) dimensions. For example, for a support made of shapeable metal having a sinusoidal or zig-zag configuration as shown FIGS. **8**C-D, a cross-sectional dimension **117** of the support can be decreased or increased by apply tension along dimension **119**. As illustrated in FIG. **10**A, a support **160** can extend essentially around the entire circumference of Schlemm's canal **30**. Alternatively, a support can extend approximately half way around the circumference of the canal (not shown). As shown in FIG. **10**B, a support **162** can extend less than halfway around the canal. As shown in FIG. **10**C, a support **164** can extend a quarter or less of the circumference around the canal. In addition, more than one support **164**, **166**, **168** can be inserted into a single Schlemm's canal. If multiple supports are inserted into a single canal, they can be of different shapes, lengths, materials or sizes.

A support can be configured such that it will open the canal beyond a maximum cross-sectional dimension of the support itself. For example, as illustrated in FIG. **11**A, device **130** comprising support **132** is inserted into Schlemm's canal **30**. Support **132** comprises beads **134** which have a maximum cross-sectional dimension B_D. Support **132** comprises a stiff arcuate element **135** with a radius of curvature R_{supp} smaller than the radius of curvature of Schlemm's canal R_{SC}. The smaller, fixed radius of curvature R_{supp} of arcuate member **135** urges canal **30** to open more than B_D. In other variations shown in FIGS. **11**B and **11**D, support **179** comprises an arcuate member **180** without beads having a radius of curvature R_{supp} that is less than the radius of curvature R_{SC} of the canal. Member **180** is sufficiently stiff to urge the canal open. In another variation shown in FIG. **11**C, support **181** comprises an arcuate member **182** having a radius of curvature R_{supp} larger than that of Schlemm's canal R_{SC}. Member **182** is also sufficiently stiff to urge the canal open. Arcuate members **135**, **180** and **182** can comprise a shape memory material such as Nitinol, for example. As indicated in FIG. **11**C, support **181** can include beads **184**. To urge open the canal, the radius of curvature R_{supp} of an arcuate members can be about 10%, 20%, 30%, 40%, or 50% or smaller or larger than that of Schlemm's canal R_{SC}. For example, an arcuate member can have a radius of curvature of about 3 mm to about 8 mm. In some variations, the radius of curvature of an arcuate member R_{supp} in a support is about 3 mm, or about 4 mm, or about 5 mm. In other variations, the radius of curvature R_{supp} of an arcuate member in a support is about 6 mm, or about 7 mm, or about 8 mm.

The supports described here occupy at least a portion of a central core of Schlemm's canal. The central core of Schlemm's canal is the region around the cross-sectional center of the canal in the interior space of the canal lumen. A support that occupies at least a portion of the central core of the canal can traverse at least a portion of the canal lumen. For example, some variations of supports can traverse the cross-sectional center of the canal at at least one point. Referring to FIG. **12**A, a front view of a support **220** having beads **222** connected with connectors **224** is provided. FIG. **12**B shows an expanded cross-sectional view along line II-II'. Support **220** occupies a portion canal central core **67** in canal lumen **64**. Trabecular meshwork **28** is shown adjacent to canal **30**. In this variation, support **220** traverses the cross-sectional center **66** of the canal. In other variations, supports can traverse the lumen of the canal off-center, e.g., appearing as a chord across the canal lumen in cross-section. Referring to FIG. **12**C, a front view of an arcuate support **210** is shown. FIG. **12**D shows an expanded cross-sectional view along line III-III'. Support **210** traverses and occupies a portion of central core **67** in lumen **64** of canal **30** without passing through canal center **66**. In some variations, the support can occupy the majority of the central core of the canal. Referring to FIG. **12**E, a front view of support **230** comprising disc-like beads **232** is shown. A cross-sectional view along line IV-IV' is shown in FIG. **12**F. As illustrated

in FIG. **12**F, bead **232** with fenestrations **234** occupies the majority of central core **67** of canal **30**. In other variations, the support occupies only a small portion of the central core of the canal. For example, in FIG. **12**G, a front view of a support **240** having an open network structure is shown. A cross-sectional view along line V-V' is shown in FIG. **12**H.

A support can made of a variety of different materials. In general, the support should comprise a biocompatible material, such as a biocompatible polymer, ceramic or ceramic composite, glass or glass composite, metal, or combinations of these materials. Examples of biocompatible metals include stainless steel, gold, silver, titanium, tantalum, platinum and alloys thereof, cobalt and chromium alloys, and titanium nickel alloys such as Nitinol. Examples of biocompatible polymers include high density polyethylene, polyurethane, polycarbonate, polypropylene, polymethylmethacrylate, polybutylmethacryate, polyesters, polytetrafluoroethylene, silicone, polyvinyl alcohol, polyvinyl pyrrolidone, polyvinyl chloride, ethyl vinyl acetate, collagen, collagen derivatives, flexible fused silica, polyolefins, NYLON® polymer, polyimide, polyacrylamide, fluorinated elastomers, and copolymers and blends thereof. In addition, biocompatible hydrogels can be used in supports and devices described herein. As discussed in more detail below, biocompatible polymers may be biodegradable. A support can be made of a single material or a combination of materials. In some variations, a support made from a first material is coated with a second material, e.g., to enhance or improve its biocompatibility.

In some examples, the biocompatible polymer in a support will include a biodegradable polymer. Examples of suitable biodegradable polymers include collagen, a collagen derivative, a poly(lactide), a poly(glycolide), a poly (lactide-co-glycolide), a poly(lactic acid), a poly(glycolic acid), a poly(lactic acid-co-glycolic acid), a poly(lactide)/poly(ethylene glycol) copolymer, a poly(glycolide)/poly (ethylene glycol) copolymer, a poly(lactide-co-glycolide)/polyethylene glycol) copolymer, a poly(lactic acid)/poly (ethylene glycol) copolymer, a poly(glycolic acid)/poly (ethylene glycol) copolymer, a poly(lactic acid-co-glycolic acid)/poly(ethylene glycol) copolymer, a poly(caprolactone), a poly(caprolactone)poly(ethylene glycol) copolymer, a polyorthoester, a poly(phosphazene), a poly(hydroxybutyrate) or a copolymer including a poly(hdroxybutyrate), a poly(lactide-co-caprolactone), a polycarbonate, a poly(esteramide), a polyanydride, a poly(dioxanone), a poly(alykylene alkylate), a copolymer of polyethylene glycol and a polyorthoester, a biodegradable polyurethane, a poly(amino acid), a polyetherester, a polyacetal, a polycyanoacrylate, a poly(oxyethylene)/poly(oxypropylene) copolymer, and blends and copolymers thereof.

At least a portion of the support can be made from a shape memory material. For example, shape memory alloys, e.g. a nickel-titanium alloy can be used. In addition, shape memory polymers, e.g., polymers made from copolymerizing monomers oligo(e-caprolactone) dimethacrylate and n-butyl acrylate or polymers based on styrene acrylate, cyanate ester and epoxies, can be used. If a shape memory material is used in the support, the support can have a compressed state prior to and during implantation, and an expanded state following implantation. The use of a compressed state support comprising a shape memory material can allow for a smaller incision and facilitate insertion into a narrowed or compressed Schlemm's canal. Once implanted, the support can be expanding using any suitable method, e.g., thermally activated by body heat or an alternate heat source, to adopt an expanded state, thereby opening the canal.

The support can include an active agent, such as a pharmaceutical. Active agents can include prostaglandins, prostaglandin analogs, beta blockers, alpha-2 agonists, calcium channel blockers, carbonic anhydrase inhibitors, growth factors, such as tissue growth factors and vascular endothelial growth factors, anti-metabolites, chemotherapeutic agents such as mitomycin-C,5-fluorouracil, steroids, antagonists of growth factors such as antagonists of vascular endothelial growth factors, or combinations thereof. The active agent can be provided as a coating on at least a portion of a support. The active agent can be delivered throughout the eye by dissolution or other dispersal mechanisms. Alternatively, at least a portion of the support can be impregnated with the active agent. In other embodiments, the active agent can be dispersed within at least a portion of the support. For example, a cavity in the support can be filled with the active agent.

The delivery of the active agent can be controlled by time-release. For example, the portion of the support containing the active agent can include a time release coating or time release formulation designed to gradually dissipate the active agent over a certain period of time. Biodegradable coatings and formulations for time-release of active agents are known in the art. In some variations, the support can comprise multiple layers, where the layers each comprise an active agent. For example, support layers can be used to release a series of different agents, or a series of doses of the same agent. Such layers can be part of a coating applied to a support, or part of a support body. In addition, the support can comprise biodegradable layers containing no active agent that can be applied or interspersed between other layers to further control delivery of active agents to the eye.

In some variations, it will be desirable to change or alter the support using electromagnetic radiation. For example, at least a portion of a support can be fenestrated, perforated, bent, shaped or formed using a laser to enhance intraocular pressure reduction. As illustrated in FIG. **13**, predetermined localized portions **120** of support **122** can be designed to absorb light of a certain wavelength or wavelength range. Preferential absorption can be achieved by material selection and/or by doping with chromophores. Upon irradiation with sufficient energy at the selected wavelength or wavelength range, the patterned regions **120** will ablate or melt, leaving new or enlarged perforations or indentations in the support. For example, a pulsed titanium sapphire laser operating between about 750 and about 800 nm can be used to ablate gold regions. If beads **126** in support **120** are hollow, then after irradiation and ablation, features **120** will become fenestrations. The fenestrations can be created to make support **122** more porous in nature or to allow release of an active agent from within a support. e.g., from within beads **126**. Alternatively, it is possible to use a mask in combination with electromagnetic radiation to alter a support, such as by patterning or machining. The modification of a support using electromagnetic radiation can be carried out prior to or subsequent to insertion.

In some variations, the visual appearance of the support can be enhanced under certain conditions to facilitate placement or to monitor the position or condition of the support. Visual enhancement can be achieved by incorporating into or onto the support chromophores that fluoresce or phosphoresce upon excitation with a light source. Chromophores can also assist a clinician in verifying the position of the support postoperatively using a gonioscope, for example.

Light sources can include lasers, lamps, and light emitting diodes. In some instances, transmission or absorption filters may be used to select the wavelength of the excitation source or to detect or view emission. Emission from a support capable of visual enhancement may be in the wavelength range of about 300 nm to about 800 nm. The chromophores can be an integral component of the material making up the support, doped into support material, or coated or sprayed onto the support. Visually-enhancing chromophores can be applied on a temporary basis, or on a permanent basis. An example of a suitable chromophore is fluorescein, which can be excited with any laser or lamp emitting at about 400 to about 500 nm. In addition, phosphorus-based chemiluminescent or photoluminscent pigments can be used, which can be selected to absorb at various wavelengths across the visible spectrum.

In some variations, the support may be capable of being attached to tissue. For example, the support may include a hook, loop, clip, extension, or the like that may be easily attached to tissue. The support may also be attached to tissue using sutures or adhesives. The support may be attached to tissue using more than one attachment method, e.g., suturing may be used in combination with a loop, or an adhesive may be used in combination with a hook. In other variations, the support may be allowed to self-position in Schlemm's canal. In still other variations, the support may be mobile within Schlemm's canal.

Kits

Kits for reducing intraocular pressure are provided, where the kits contain at least one support that can be implanted circumferentially within Schlemm's canal configured to maintain the patency of at least a portion of Schlemm's canal. The support occupies at least a portion of a central core of Schlemm's canal and does not substantially interfere with transmural flow across the canal. The kits also provide an introducer or delivery device for implanting the support in the canal. The support and introducer are provided in packaged combination in the kits. The kits can also include instructions for use, e.g., for implanting and inspecting the support.

The introducer can be inserted into the eye and is capable of implanting the support at the desired implantation position within Schlemm's canal. For example, an introducer may include a tubular cannula through which the support may be passed. In addition to a cannula, the introducer may include a tubular or solid pusher rod that can be used to push or advance the support into and/or around Schlemm's canal. Alternatively, a pusher rod or plunger can be used without a cannula to introduce a support into the canal. A support can be installed into the lumen of a cannula prior to insertion, the distal end of the cannula positioned at or near the desired support location, and the pusher rod operated from the proximal end to push the support distally out of the distal end of the cannula and into the canal. The cannula and/or the pusher rod may be flexible and small enough in diameter to extend at least partially around the canal. In some variations, a proximal end of a suture can be introduced into the canal via a cannula and the suture extended circumferentially around the canal. A distal portion of the suture can be connected to the support and force applied to the proximal end of the suture to pull the support into the canal. The support can then be positioned within the canal by pulling the suture in a distal or proximal direction. The suture can be used to anchor the support within the canal. In other variations, the support can be directly introduced into the canal using surgical forceps, or the like.

FIGS. **14**A-D illustrate additional variations for introducing a support into the canal. As shown in FIG. **14**A, a support **200** can be introduced into the canal using syringe **202** and plunger **204**. Syringe **202** has distal end **206** that can be at least partially inserted into or placed adjacent to an opening in the canal. Force in a distal direction is applied to plunger **204**, thereby pushing support **200** into the canal. Referring to FIGS. **14**B-C, distal end **208** of guide element **210** can be at least partially introduced into the canal. Guide element **210** can be a guide wire. Guide element **210** can be extended circumferentially along the canal to aid in positioning the support. Support **212** comprises central bore **218** capable of accommodating guide element **210** such that support **212** can be threaded onto guide element **210** and slidably positioned along the guide element. Once distal end **209** of support **212** is threaded onto guide element **210**, support **212** can be pushed in a distal direction along guide element **210** to insert support **212** into the canal. In some variations, support **212** can remain threaded onto guide element **210**, and guide element **210** can remain in the canal. In other variations, support **212** can be slid off distal end **208** of guide element **210**, and the guide element can be pulled in a proximal direction for removal. Referring to FIGS. **14**C-D, syringe **202** with plunger **204** can be used in combination with a guide element **210**. In this variation, distal end **208** of guide element **210** is inserted at least partially into Schlemm's canal. Guide element **210** can be extended circumferentially along the canal to aid in positioning the support. Support **212** has central bore **218** capable of accommodating guide element **210**. Proximal end **211** of guide element **210** is inserted into bore **218**. Plunger **204** is depressed in a distal direction to push support **212** into the canal and slide support **212** along element **210**. Guide element **210** can remain in the canal or be removed following insertion of the support. Supports **200**, **212** must be sufficiently resilient to withstand force encountered as they are pushed into the canal.

In some variations, a positioning device may be used with the introducer to position or adjust the support within the canal. A positioning device can include a rod, grippers, a clamp, a hook, or the like. In other variations, a device or system capable of dilating the canal to facilitate insertion of a support may be included in the kits, e.g., a syringe or other device capable of injecting fluid into the canal.

In some variations, the kits contain at least two supports. Multiple supports can be implanted within one eye or within multiple eyes. If the kits contain multiple supports, the kits may also contain multiple introducers. Alternatively, the same introducer may be used for implantation of multiple supports, especially if the multiple supports are being delivered to a single eye. If multiple supports are to be delivered with the same introducer, then the multiple supports can be preloaded into the introducer for sterility. If more than one support is included in a kit, the supports may be of different shapes, sizes, lengths, or materials. If the kits contain more than one support to be implanted into a single eye, the supports can be connected together.

The kits can comprise an active agent, such as a pharmaceutical agent. The active agent may be included as an integral part of the support, or may be supplied in kits for application to the support or to the eye during or after implantation. Examples of active agents that may be supplied as part of the kits include prostaglandins, prostaglandin analogs, beta blockers, alpha-2 agonists, calcium channel blockers, carbonic anhydrase inhibitors, growth factors, such as tissue growth factors or vascular endothelial growth factors, anti-metabolites, chemotherapeutic agents such as

mitomycin-C,5-fluorouracil, steroids, antagonists of growth factors, such as antagonists of vascular endothelial growth factor, and combinations thereof.

The kits may contain a fixation device for attaching a support to tissue. Such a fixation device can include sutures, hooks, barbs, clips, adhesives, and combinations thereof. In addition, the kits may include a system for visually enhancing the support to facilitate viewing, positioning, and monitoring of a support. A system for visually enhancing the support can include a light source, a transmission or absorption filter, a mirror, a composition comprising a chromophore capable of fluorescing or phosphorescing that can be applied to the support, or any combination thereof. Chromophores can assist a clinician in verifying the position of the support postoperatively using a gonioscope, for example. The light source is capable of exciting a chromophore contained within or on the support such that the chromophore emits fluorescence or phosphorescence. The emission is preferably within the wavelength range of about 300 nm to about 800 nm. A suitable light source for such a system can comprise a laser, a light emitting diode, or a lamp. In some instances, transmission or absorption filters may be used to further select the wavelength range of the excitation source or view or detect emission from chromophores. One or more mirrors may be used to direct a light source or emitted light, or to view the support.

Methods

Methods for reducing intraocular pressure are also provided. In general, the methods comprise inserting a support circumferentially within Schlemm's canal, such that the support maintains the patency of at least a portion of the canal. The support occupies at least a portion of a central core of Schlemm's canal and does not substantially interfere with transmural flow across Schlemm's canal.

The methods can comprise inserting a support circumferentially into Schlemm's canal using an introducer and/or a positioning device. The introducer can include a cannula and a tubular or hollow pusher rod. The support can be installed in the lumen of the cannula at its distal end and the pusher rod can be inserted into the lumen of the cannula at its proximal end and extended distally to push the support into position in the canal. In some instances, the cannula and/or the pusher rod may be flexible and small enough in diameter to at least partially extend circumferentially around the canal. In some variations of the methods, a positioning device can be used in addition to an introducer. The positioning device can comprise a second rod, a gripper, a hook, a clamp, or the like. In some variations, the methods include illuminating a support with a light source to causes the support to fluoresce or phosphoresce, thus aiding the visual appearance of the support. The illuminating of the support can occur during or after implantation to inspect the support, e.g., to monitor its position, condition, or performance.

In some instances, the methods will also comprise dilating Schlemm's canal prior to insertion of the support. Dilation of the canal can be accomplished by injecting fluid into the canal. For example, a high viscosity fluid such as sodium hyaluronate, or other dilating fluids known in the art, can be used to dilate the canal.

The methods may include implanting more than one support into an eye. In some variations, the methods will include implantation of two or more supports circumferentially adjacent to each other within the canal, and in other variations, the methods will include implantation of supports circumferentially opposed to each other within the canal, e.g., two supports centered about 180° apart around the circumference of Schlemm's canal. Some variations of the methods can comprise connecting together multiple supports in a single eye.

In some variations, the methods can include anchoring the support to tissue surrounding Schlemm's canal. Anchoring the support to tissue can be accomplished in a variety of ways, e.g., by suturing, application of adhesives, installation of hooks, clips, or the like, or combinations thereof. In other variations, the methods can comprise selecting the size of the support such that the support fits securely into the canal by a friction fit. Examples of arcuate supports that can be implanted with a friction fit are illustrated in FIGS. **11**A-C.

The methods described here can also include altering the support using electromagnetic radiation. For example, a support can include regions capable of preferentially absorbing a certain wavelength range. When electromagnetic radiation of the appropriate wavelength range with sufficient energy is incident upon the support, material in the preferentially absorbing regions will melt or ablate, resulting in perforations or indentations in the support at those regions. For example, a pulsed titanium sapphire laser emitting at about 750 nm to about 800 nm incident on gold can cause the gold to melt or ablate. The alteration of the support using electromagnetic radiation can occur before or after implantation of a support. For example, fenestrations can be created or enlarged in a support after the support has remained in an eye for a period of time to enhance drainage.

While the inventive devices, kits and methods have been described in some detail by way of illustration, such illustration is for purposes of clarity of understanding only. It will be readily apparent to those of ordinary skill in the art in light of the teachings herein that certain changes and modifications may be made thereto without departing from the spirit and scope of the appended claims. For example, it is envisioned that the devices, kits and methods can be applied to nonhuman eyes to reduce intraocular pressure, e.g., in dogs, cats, primates, or horses.

The invention claimed is:

1. A method for reducing intraocular pressure in a patient using a support and an introducer comprising a cannula, comprising:

positioning a distal end of the cannula at or near Schlemm's canal, wherein the support is located in a lumen of the cannula; and

pushing the support distally out of the distal end of the cannula to insert the support circumferentially within Schlemm's canal,

wherein the support comprises an arcuate member, wherein at least a portion of the arcuate member has a radius of curvature R_{supp} smaller than the radius of curvature of Schlemm's canal such that at least a portion of the arcuate member extends out of Schlemm's canal.

2. The method of claim **1**, wherein the patient has glaucoma.

3. The method of claim **1**, further comprising anchoring the support to tissue surrounding Schlemm's canal.

4. The method of claim **1**, further comprising dilating Schlemm's canal prior to inserting the support.

5. The method of claim **4**, wherein Schlemm's canal is dilated by injecting fluid into the canal.

6. The method of claim **1**, wherein the support at least partially props open Schlemm's canal.

7. The method of claim **1**, wherein the support does not significantly block fluid outflow to the collector channels after insertion into Schlemm's canal.

8. The method of claim **1**, wherein the support does not significantly block fluid outflow from the trabecular meshwork after insertion into Schlemm's canal.

9. The method of claim **1**, wherein R_{supp} is about 10% smaller than the radius of curvature of Schlemm's canal.

10. The method of claim **1**, wherein R_{supp} is about 20% smaller than the radius of curvature of Schlemm's canal.

11. The method of claim **1**, wherein R_{supp} is about 30% smaller than the radius of curvature of Schlemm's canal.

12. The method of claim **1**, wherein R_{supp} is about 40% smaller than the radius of curvature of Schlemm's canal.

13. The method of claim **1**, wherein R_{supp} is about 50% smaller than the radius of curvature of Schlemm's canal.

14. The method of claim **1**, wherein R_{supp} is about 3 mm.

15. The method of claim **1**, wherein R_{supp} is about 4 mm.

16. The method of claim **1**, wherein R_{supp} is about 5 mm.

17. The method of claim **1**, wherein the support extends less than a quarter of the way around Schlemm's canal after insertion into the canal.

18. The method of claim **1**, wherein the support extends about one quarter of the way around Schlemm's canal after insertion into the canal.

19. The method of claim **1**, wherein the support extends about one half of the way around Schlemm's canal after insertion into the canal.

20. The method of claim **1**, wherein the support extends about all the way around Schlemm's canal after insertion into the canal.

21. The method of claim **1**, wherein when the support is inserted within a cylindrical section of the lumen of Schlemm's canal having an internal wall surface area C, the support contacts less than 30% of the surface area of C.

22. The method of claim **1**, wherein the support comprises at least one fenestration.

23. The method of claim **1**, wherein the support comprises a plurality of fenestrations.

24. The method of claim **1**, wherein the support is non-tubular.

25. The method of claim **1**, wherein the support comprises a shape memory alloy.

26. The method of claim **1**, wherein the support has a first shape prior to insertion within Schlemm's canal and a second shape after insertion.

27. The method of claim **1**, wherein the support has a sinusoidal shape.

* * * * *

EXHIBIT 6

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
15/182,165	06/14/2016	David Y. BADAWI	SGHT-001/05US 328518-2019	4703

58249 7590 08/09/2018

COOLEY LLP
ATTN: IP Docketing Department
1299 Pennsylvania Avenue, NW
Suite 700
Washington, DC 20004

EXAMINER
DEAK, LESLIE R

ART UNIT	PAPER NUMBER
3761	

NOTIFICATION DATE	DELIVERY MODE
08/09/2018	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

zIPPatentDocketingMailboxUS@cooley.com

Office Action Summary	Application No.	Applicant(s)	
	15/182,165	BADAWI ET AL.	
	Examiner	Art Unit	
	LESLIE DEAK	3761	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 June 2016*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *14 June 2016* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The present application is being examined under the pre-AIA first to invent provisions.

Drawings

2. The drawings are objected to under 37 CFR 1.83(a). The drawings must show every feature of the invention specified in the claims. Therefore, the portion of the support that is configured to extend out of Schlemm's canal as recited in claim 21, must be shown or the feature(s) canceled from the claim(s). No new matter should be entered.

Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner,

the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112(a):

> (a) IN GENERAL.—The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor or joint inventor of carrying out the invention.

The following is a quotation of the first paragraph of pre-AIA 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 21-40 are rejected under 35 U.S.C. 112(a) or 35 U.S.C. 112 (pre-AIA), first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor or a joint inventor, or for pre-AIA the inventor(s), at the time the application was filed, had possession of the claimed invention. The Specification discloses that the implant may extend partially beyond Schlemm's canal (paragraph 0041), but does not describe what form that extension may take. Similarly, the Specification discloses that the implant may comprise a radius of curvature smaller or larger than the radius of curvature of Schlemm's canal (paragraph 0054), but does not teach that these radii are the means

by which the implant extends beyond Schlemm's canal. Applicant appears to be attempting to combine two separate embodiments of the invention in a single embodiment, which is not adequately described in the Specification.

Double Patenting

5. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on nonstatutory double patenting provided the reference application or patent either is shown to be commonly owned with the examined application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement. See

MPEP § 717.02 for applications subject to examination under the first inventor to file provisions of the AIA as explained in MPEP § 2159. See MPEP §§ 706.02(l)(1) - 706.02(l)(3) for applications not subject to examination under the first inventor to file provisions of the AIA. A terminal disclaimer must be signed in compliance with 37 CFR 1.321(b).

The USPTO Internet website contains terminal disclaimer forms which may be used. Please visit www.uspto.gov/patent/patents-forms. The filing date of the application in which the form is filed determines what form (e.g., PTO/SB/25, PTO/SB/26, PTO/AIA/25, or PTO/AIA/26) should be used. A web-based eTerminal Disclaimer may be filled out completely online using web-screens. An eTerminal Disclaimer that meets all requirements is auto-processed and approved immediately upon submission. For more information about eTerminal Disclaimers, refer to www.uspto.gov/patents/process/file/efs/guidance/eTD-info-I.jsp.

6. Claims 21, 22, 37, and 38 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 6, 7, and 9 of U.S. Patent No. 9,486,361 to Badawi et al. Although the claims at issue are not identical, they are not patentably distinct from each other because the more detailed method set forth in the ‘361 patent anticipates the instantly claimed method.

7. Claims 23-36, 39-40 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 6, 7, and 9 of U.S. Patent No. 9,486,361 to Badawi et al in view of claims 1, 12-15, 21-23, 27, 45, 46, 50, 52, 53, 70, and 71 of U.S. Patent No. 9,370,443 to Badawi et al. Although the claims at issue are not identical, they are

not patentably distinct from each other because the more detailed method set forth in the '361 patent anticipates the method set forth in claim 21, and the rest of the claims recite limitations drawn to the structure of the implant itself, which are found in the claims of the '443 patent.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LESLIE DEAK whose telephone number is (571)272-4943. The examiner can normally be reached on Monday - Friday, 8:30am-5:00pm.

Examiner interviews are available via telephone, in-person, and video conferencing using a USPTO supplied web-based collaboration tool. To schedule an interview, applicant is encouraged to use the USPTO Automated Interview Request (AIR) at http://www.uspto.gov/interviewpractice.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Tanya Zalukaeva can be reached on 571-272-1115. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/LESLIE DEAK/
Primary Examiner, Art Unit 3761
31 July 2018

EXHIBIT 7

Docket No.: SGHT-001/05US 328518-2019
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Inventor:	David Y. BADAWI	Confirmation No.:	4703
Application No.:	15/182,165	Group Art Unit:	3781
Filed:	June 14, 2016	Examiner:	Leslie R. Deak

For: INTRAOCULAR IMPLANTS AND METHODS AND KITS THEREFOR

AMENDMENT/RESPONSE TO NON-FINAL OFFICE ACTION

MS Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

INTRODUCTORY COMMENTS

This is in response to the non-final Office Action dated August 9, 2018, for which a response was due on November 9, 2018. Applicant hereby petitions for a one (1) month extension of time, thereby extending the deadline for response from November 9, 2018, up to and including December 9, 2018, which was a Sunday. Pursuant to 37 C.F.R. 1.7(a), when a filing deadline in the Patent and Trademark Office falls on Saturday, Sunday, or a Federal holiday, the action may be taken on the next succeeding day which is not a Saturday, Sunday, or a Federal holiday. Accordingly, this response is timely filed. Also filed herewith is a supplemental Information Disclosure Statement. Reconsideration and allowance of the pending claims, as amended, in light of the remarks presented herein are respectfully requested.

Amendments to the Specification begin on page **3** of this paper.

Amendments to the Claims are reflected in the listing of the claims which begins on page **5** of this paper.

Amendments to the Drawings appear on page **8** of this paper.

Remarks/Arguments begin on page **9** of this paper.

PTO/AIA/26 (04-14)
Approved for use through 11/30/2020. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

TERMINAL DISCLAIMER TO OBVIATE A DOUBLE PATENTING REJECTION OVER A "PRIOR" PATENT

Docket Number (Optional)
SGHT-001/05US 328518-2019

In re Application of: David Y. BADAWI et al.

Application No.: 15/182,165

Filed: June 14, 2016

For: INTRAOCULAR IMPLANTS AND METHODS AND KITS THEREFOR

The applicant, Sight Sciences, Inc., owner of 100 percent interest in the instant application hereby disclaims, except as provided below, the terminal part of the statutory term of any patent granted on the instant application which would extend beyond the expiration date of the full statutory term of **prior patent** No. (see attached) as the term of said **prior patent** is presently shortened by any terminal disclaimer. The applicant hereby agrees that any patent so granted on the instant application shall be enforceable only for and during such period that it and the **prior patent** are commonly owned. This agreement runs with any patent granted on the instant application and is binding upon the grantee, its successors or assigns.

In making the above disclaimer, the applicant does not disclaim the terminal part of the term of any patent granted on the instant application that would extend to the expiration date of the full statutory term of the **prior patent**, "as the term of said **prior patent** is presently shortened by any terminal disclaimer," in the event that said **prior patent** later:

expires for failure to pay a maintenance fee;
is held unenforceable;
is found invalid by a court of competent jurisdiction;
is statutorily disclaimed in whole or terminally disclaimed under 37 CFR 1.321;
has all claims canceled by a reexamination certificate;
is reissued; or
is in any manner terminated prior to the expiration of its full statutory term as presently shortened by any terminal disclaimer.

Check either box 1 or 2 below, if appropriate.

1. ☐ The undersigned is the applicant. If the applicant is an assignee, the undersigned is authorized to act on behalf of the assignee.

I hereby acknowledge that any willful false statements made are punishable under 18 U.S.C. 1001 by fine or imprisonment of not more than five (5) years, or both.

2. ☒ The undersigned is an attorney or agent of record. Reg. No. 70,897

/Amy Motomura/ — Signature
December 10, 2018 — Date

Amy Motomura — Typed or printed name

Attorney for Applicant — Title
(415) 693-2048 — Telephone Number

☒ Terminal disclaimer fee under 37 CFR 1.20(d) included.

WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

SUPPLEMENTAL SHEET FOR USE WITH PTO/AIA/26 (04-14)

SUPPLEMENTAL SHEET FOR TERMINAL DISCLAIMER TO OBVIATE A DOUBLE PATENTING REJECTION OVER A "PRIOR" PATENT	Docket Number (Optional) SGHT-001/05US 328518-2019

Prior patent Nos. applicable to this terminal disclaimer (referenced on first page):

9,486,361
9,370,443

EXHIBIT 8

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
16/413,466	05/15/2019	David Y. BADAWI	SGHT-001/07US 328518-2065	9572

58249 7590 04/26/2022

COOLEY LLP
ATTN: IP Docketing Department
1299 Pennsylvania Avenue, NW
Suite 700
Washington, DC 20004

EXAMINER	
DEAK, LESLIE R	

ART UNIT	PAPER NUMBER
3799	

NOTIFICATION DATE	DELIVERY MODE
04/26/2022	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

zIPPatentDocketingMailboxUS@cooley.com

Office Action Summary	Application No. 16/413,466	Applicant(s) BADAWI et al.	
	Examiner LESLIE R DEAK	Art Unit 3799	AIA (FITF) Status No

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTHS FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☑ Responsive to communication(s) filed on 24 October 2019.

☐ A declaration(s)/affidavit(s) under **37 CFR 1.130(b)** was/were filed on _____.

2a)☐ This action is **FINAL.** 2b) ☑ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims*

5) ☑ Claim(s) 21-47 is/are pending in the application.

5a) Of the above claim(s) _____ is/are withdrawn from consideration.

6) ☐ Claim(s) _____ is/are allowed.

7) ☑ Claim(s) 21-47 is/are rejected.

8) ☐ Claim(s) _____ is/are objected to.

9) ☐ Claim(s) _____ are subject to restriction and/or election requirement

* If any claims have been determined allowable, you may be eligible to benefit from the **Patent Prosecution Highway** program at a participating intellectual property office for the corresponding application. For more information, please see http://www.uspto.gov/patents/init_events/pph/index.jsp or send an inquiry to **PPHfeedback@uspto.gov.**

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☑ The drawing(s) filed on 15 May 2019 is/are: a)☑ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

Certified copies:

a)☐ All b)☐ Some** c)☐ None of the:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

** See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☑ Notice of References Cited (PTO-892)

2) ☑ Information Disclosure Statement(s) (PTO/SB/08a and/or PTO/SB/08b) Paper No(s)/Mail Date _____.

3) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date _____.

4) ☐ Other: _____.

DETAILED ACTION

1. The present application is being examined under the pre-AIA first to invent provisions.

Double Patenting

2. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on nonstatutory double patenting provided the reference application or patent either is shown to be commonly owned with the examined application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement. See MPEP § 717.02 for applications subject to examination under the first inventor to file provisions of the AIA as explained in MPEP § 2159. See MPEP §§ 706.02(l)(1) -

706.02(l)(3) for applications not subject to examination under the first inventor to file provisions of the AIA. A terminal disclaimer must be signed in compliance with 37 CFR 1.321(b).

The USPTO Internet website contains terminal disclaimer forms which may be used. Please visit www.uspto.gov/patent/patents-forms. The filing date of the application in which the form is filed determines what form (e.g., PTO/SB/25, PTO/SB/26, PTO/AIA/25, or PTO/AIA/26) should be used. A web-based eTerminal Disclaimer may be filled out completely online using web-screens. An eTerminal Disclaimer that meets all requirements is auto-processed and approved immediately upon submission. For more information about eTerminal Disclaimers, refer to www.uspto.gov/patents/process/file/efs/guidance/eTD-info-I.jsp.

3. Claims 21, 22 45 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 6, 20 of U.S. Patent No.10,314,742 to Badawi et al. Although the claims at issue are not identical, they are not patentably distinct from each other because each method sets forth the step of using a cannula to introduce an arcuate support into Schlemm's canal wherein the support comprises a specific radius of curvature.

With regard to claim 22, it is well known in the art that a patient experiencing glaucoma benefits from a reduction in ocular pressure, rendering the patient selection step patentably indistinct from the prior art.

With regard to claims 29-36 and 40, Badawi '742 does not recite the instantly claimed dimensions. However, it has been held that where the only difference between

the prior art and the claims was a recitation of relative dimensions of the claimed device and a device having the claimed relative dimensions would not perform differently than the prior art device, the claimed device was not patentably distinct from the prior art device. See MPEP 2144.04(IV)(B). As such the limitations are patentably indistinct from the prior art.

4. Claims 22, 23, are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 2, 3 of U.S. Patent No. 7,909,789 to Badawi et al in view of claim 40 of U.S. Patent No.10,314,742 to Badawi et al. Although the claims at issue are not identical, they are not patentably distinct from each other because The '789 method sets forth the details of the instantly claimed implantation method, whereas the '742 method sets forth the location of the support with regard to Schlemm's canal. Taken together, the patented claims suggest the instantly claimed method.

5. Claims 26-28, 37-38, 39, 42-44, 46, 47 are rejected on the ground of nonstatutory double patenting as being unpatentable over claims 1, 12, 11, 25, 34, 41 of U.S. Patent No. 9,370,443 to Badawi et al in view of claim 40 of U.S. Patent No.10,314,742 to Badawi et al. Although the claims at issue are not identical, they are not patentably distinct from each other because The '789 method sets forth the details of the instantly claimed implant, whereas the '742 method sets forth the location of the support with regard to Schlemm's canal. Taken together, the patented claims suggest the instantly claimed method.

6. Claims 21, 24, 25 are rejected on the ground of nonstatutory double patenting as being unpatentable over claim 1 of U.S. Patent No. 9,486,361 to Badawi et al in view of claim 40 of U.S. Patent No.10,314,742 to Badawi et al. Although the claims at issue are not identical, they are not patentably distinct from each other because The '789 method sets forth the details of the instantly claimed implant, whereas the '742 method sets forth the location of the support with regard to Schlemm's canal. Taken together, the patented claims suggest the instantly claimed method.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LESLIE R DEAK whose telephone number is (571)272-4943. The examiner can normally be reached on Monday-Friday, 9am to 5:30pm.

Examiner interviews are available via telephone, in-person, and video conferencing using a USPTO supplied web-based collaboration tool. To schedule an interview, applicant is encouraged to use the USPTO Automated Interview Request (AIR) at http://www.uspto.gov/interviewpractice.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Tom Sweet can be reached on 571-272-4761. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/LESLIE R DEAK/
Primary Examiner, Art Unit 3799
21 April 2022

EXHIBIT 9

Docket No.: SGHT-001/07US 328518-2065
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

First Inventor:	David Y. BADAWI	Confirmation No.:	9572
Application No.:	16/413,466	Group Art Unit:	3799
Filed:	May 15, 2019	Examiner:	Leslie R. Deak

For: INTRAOCULAR IMPLANTS AND METHODS AND KITS THEREFOR

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

RESPONSE TO NON-FINAL OFFICE ACTION

This is in response to the non-final Office Action dated April 26, 2022, for which a response is due on July 26, 2022. Accordingly, this response is timely filed. Also filed concurrently herewith are a Terminal Disclaimer and a supplemental Information Disclosure Statement. Allowance of the pending claims in light of the remarks presented herein is respectfully requested.

Claims begin on page 2 of this paper.

Remarks/Arguments begin on page 5 of this paper.

IN THE CLAIMS:

Set forth below in ascending order, with status identifiers, is a complete listing of all claims currently under examination. Changes to any amended claims are indicated by [[double brackets]], ~~strikethrough~~ and/or underlining. This listing also reflects any cancellation and/or addition of claims.

Claims 1-20 (Cancelled).

Claim 21 (Previously Presented): A method for reducing intraocular pressure in a patient using a support and an introducer comprising a cannula, comprising:

positioning a distal end of the cannula at or near Schlemm's canal, wherein the support is located in a lumen of the cannula; and

pushing the support distally out of the distal end of the cannula to insert the support circumferentially within Schlemm's canal,

wherein the support comprises an arcuate member, wherein at least a portion of the arcuate member has a radius of curvature R_{supp} smaller than the radius of curvature of Schlemm's canal such that at least a portion of the arcuate member extends out of Schlemm's canal.

Claim 22 (Previously Presented): The method of claim 21, wherein the patient has glaucoma.

Claim 23 (Previously Presented): The method of claim 21, further comprising anchoring the support to tissue surrounding Schlemm's canal.

Claim 24 (Previously Presented): The method of claim 21, further comprising dilating Schlemm's canal prior to inserting the support.

Claim 25 (Previously Presented): The method of claim 24, wherein Schlemm's canal is dilated by injecting fluid into the canal.

Claim 26 (Previously Presented): The method of claim 21, wherein the support at least partially props open Schlemm's canal.

Claim 27 (Previously Presented): The method of claim 21, wherein the support does not significantly block fluid outflow to the collector channels after insertion into Schlemm's canal.

Claim 28 (Previously Presented): The method of claim 21, wherein the support does not significantly block fluid outflow from the trabecular meshwork after insertion into Schlemm's canal.

Claim 29 (Previously Presented): The method of claim 21, wherein R_{supp} is about 10% smaller than the radius of curvature of Schlemm's canal.

Claim 30 (Previously Presented): The method of claim 21, wherein R_{supp} is about 20% smaller than the radius of curvature of Schlemm's canal.

Claim 31 (Previously Presented): The method of claim 21, wherein R_{supp} is about 30% smaller than the radius of curvature of Schlemm's canal.

Claim 32 (Previously Presented): The method of claim 21, wherein R_{supp} is about 40% smaller than the radius of curvature of Schlemm's canal.

Claim 33 (Previously Presented): The method of claim 21, wherein R_{supp} is about 50% smaller than the radius of curvature of Schlemm's canal.

Claim 34 (Previously Presented): The method of claim 21, wherein R_{supp} is about 3 mm.

Claim 35 (Previously Presented): The method of claim 21, wherein R_{supp} is about 4 mm.

Claim 36 (Previously Presented): The method of claim 21, wherein R_{supp} is about 5 mm.

Claim 37 (Previously Presented): The method of claim 21, wherein the support extends less than a quarter of the way around Schlemm's canal after insertion into the canal.

Claim 38 (Previously Presented): The method of claim 21, wherein the support extends about one quarter of the way around Schlemm's canal after insertion into the canal.

Claim 39 (Previously Presented): The method of claim 21, wherein the support extends about one half of the way around Schlemm's canal after insertion into the canal.

Claim 40 (Previously Presented): The method of claim 21, wherein the support extends about all the way around Schlemm's canal after insertion into the canal.

Claim 41 (Previously Presented): The method of claim 21, wherein when the support is inserted within a cylindrical section of the lumen of Schlemm's canal having an internal wall surface area C, the support contacts less than 30% of the surface area of C.

Claim 42 (Previously Presented): The method of claim 21, wherein the support comprises at least one fenestration.

Claim 43 (Previously Presented): The method of claim 21, wherein the support comprises a plurality of fenestrations.

Claim 44 (Previously Presented): The method of claim 21, wherein the support is non-tubular.

Claim 45 (Previously Presented): The method of claim 21, wherein the support comprises a shape memory alloy.

Claim 46 (Previously Presented): The method of claim 21, wherein the support has a first shape prior to insertion within Schlemm's canal and a second shape after insertion.

Claim 47 (Previously Presented): The method of claim 21, wherein the support has a sinusoidal shape.

REMARKS

Claims 21-47 are pending in the present application. Claims 1-20 were previously cancelled without prejudice. In this response, no claims have been amended, cancelled, or added. Accordingly, claims 21-47 are currently under consideration. Amendment and cancellation of certain claims is not to be construed as a dedication to the public of any of the subject matter of the claims as previously presented. No new matter has been added.

Double Patenting

Claims 21-22, 29-36, 40, and 45 stand rejected on the ground of nonstatutory double patenting as allegedly unpatentable over claims 6 and 20 of U.S. Patent No. 10,314,742. Claims 22-23 stand rejected on the ground of nonstatutory double patenting as allegedly unpatentable over claims 2-3 of U.S. Patent No. 7,909,789 in view of claim 40 of U.S. Patent No. 10,314,742. Claims 26-28, 37-39, 42-44, and 46-47 stand rejected on the ground of nonstatutory double patenting as allegedly unpatentable over claims 1, 12, 11, 25, 34, and 41 of U.S. Patent No. 9,370,443 in view of claim 40 of U.S. Patent No. 10,314,742. Claims 21 and 24-25 stand rejected on the ground of nonstatutory double patenting as allegedly unpatentable over claim 1 of U.S. Patent No. 9,486,361 in view of claim 40 of U.S. Patent No. 10,314,742.

Without acquiescence to these rejections, and solely to obviate the rejections, Applicant submits herewith a Terminal Disclaimer, which disclaims (except as noted) the terminal part of the statutory term of any patent granted on the instant application which would extend beyond the expiration date of the full statutory term of U.S. Patent Nos. 10,314,742, 7,909,789, 9,370,443, and 9,486,361. Accordingly, Applicant respectfully requests that the rejection of the claims 21-47 on the ground of nonstatutory obviousness-type double patenting be withdrawn.

CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejections of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

Any remarks in support of patentability of one claim should not be imputed to any other claim, even if similar terminology is used. Additionally, any remarks referring to only a portion of a claim should not be understood to base patentability on that portion; rather, patentability must rest on each claim taken as a whole. Applicant respectfully traverses each of the Examiner's rejections and each of the Examiner's assertions regarding what the prior art shows or teaches, even if not expressly discussed herein. Although amendments have been made, no acquiescence or estoppel is or should be implied thereby. Rather, the amendments are made only to expedite prosecution of the present application, and without prejudice to presentation or assertion, in the future, of claims on the subject matter affected thereby.

Although the present communication may include alterations to the application or claims, or characterizations of claim scope or referenced art, Applicant is not conceding in this application that previously pending claims are not patentable over the cited references. Rather, any alterations or characterizations are being made to facilitate expeditious prosecution of this application. Applicant reserves the right to pursue at a later date any previously pending or other broader or narrower claims that capture any subject matter supported by the present disclosure, including subject matter found to be specifically disclaimed herein or by any prior prosecution. Accordingly, reviewers of this or any parent, child, or related prosecution history shall not reasonably infer that Applicant has made any disclaimers or disavowals of any subject matter supported by the present application.

In the event the U.S. Patent and Trademark Office determines that an extension and/or other relief is required, Applicant petitions for any required relief including extensions of time

and authorizes the Director to charge any appropriate fees under 37 C.F.R. §§1.16, 1.17, and 1.21 that may be required by this paper, and to credit any overpayment, to **Deposit Account No. 50-1283** referencing docket no. SGHT-001/07US 328518-2065. However, the Director is not authorized to charge the cost of the issue fee to the Deposit Account.

Dated: May 19, 2022

Respectfully submitted,
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Doc Code: DIST.E.FILE
Document Description: Electronic Terminal Disclaimer - Filed

PTO/SB/26
U.S. Patent and Trademark Office
Department of Commerce

Electronic Petition Request	**TERMINAL DISCLAIMER TO OBVIATE A DOUBLE PATENTING REJECTION OVER A "PRIOR" PATENT**
Application Number	16413466
Filing Date	15-May-2019
First Named Inventor	David BADAWI
Attorney Docket Number	SGHT-001/07US 328518-2065
Title of Invention	INTRAOCULAR IMPLANTS AND METHODS AND KITS THEREFOR

☒ Filing of terminal disclaimer does not obviate requirement for response under 37 CFR 1.111 to outstanding Office Action

☒ This electronic Terminal Disclaimer is not being used for a Joint Research Agreement.

Owner	Percent Interest
Sight Sciences, Inc.	100%

The owner(s) with percent interest listed above in the instant application hereby disclaims, except as provided below, the terminal part of the statutory term of any patent granted on the instant application which would extend beyond the expiration date of the full statutory term of prior patent number(s)

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as the term of said prior patent is presently shortened by any terminal disclaimer. The owner hereby agrees that any patent so granted on the instant application shall be enforceable only for and during such period that it and the prior patent are commonly owned. This agreement runs with any patent granted on the instant application and is binding upon the grantee, its successors or assigns.

In making the above disclaimer, the owner does not disclaim the terminal part of the term of any patent granted on the instant application that would extend to the expiration date of the full statutory term of the prior patent, "as the term of said prior patent is presently shortened by any terminal disclaimer," in the event that said prior patent later:
- expires for failure to pay a maintenance fee;
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- is statutorily disclaimed in whole or terminally disclaimed under 37 CFR 1.321;
- has all claims canceled by a reexamination certificate;
- is reissued; or
- is in any manner terminated prior to the expiration of its full statutory term as presently shortened by any terminal disclaimer.

(●) Terminal disclaimer fee under 37 CFR 1.20(d) is included with Electronic Terminal Disclaimer request.

( ) I certify, in accordance with 37 CFR 1.4(d)(4), that the terminal disclaimer fee under 37 CFR 1.20(d) required for this terminal disclaimer has already been paid in the above-identified application.

Applicant claims the following fee status:

(●) Small Entity

( ) Micro Entity

( ) Regular Undiscounted

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

THIS PORTION MUST BE COMPLETED BY THE SIGNATORY OR SIGNATORIES

I certify, in accordance with 37 CFR 1.4(d)(4) that I am:

(●) An attorney or agent registered to practice before the Patent and Trademark Office who is of record in this application

Registration Number 71499

( ) A sole inventor

( ) A joint inventor; I certify that I am authorized to sign this submission on behalf of all of the inventors as evidenced by the power of attorney in the application

( ) A joint inventor; all of whom are signing this request

Signature	/Joanna Liebes Hubberts/
Name	Joanna Liebes Hubberts

*Statement under 37 CFR 3.73(b) is required if terminal disclaimer is signed by the assignee (owner).
Form PTO/SB/96 may be used for making this certification. See MPEP § 324.

Doc Code: DISQ.E.FILE
Document Description: Electronic Terminal Disclaimer – Approved

Application No.: 16413466

Filing Date: 15-May-2019

Applicant/Patent under Reexamination: BADAWI

Electronic Terminal Disclaimer filed on May 19, 2022

☒ APPROVED

This patent is subject to a terminal disclaimer

☐ DISAPPROVED

Approved/Disapproved by: Electronic Terminal Disclaimer automatically approved by EFS-Web

U.S. Patent and Trademark Office